Urinary incontinence in pregnancy and postpartum

Incidence, prevalence and risk factors

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Acknowledgements

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Abbreviations

CI	Confidence interval
CS	Cesarean section
BMI	Body mass index (kg/m^2)
MoBa	The Norwegian Mother and Child Cohort study
MBRN	The Medical Birth Registry of Norway
OR	Odds ratio
RR	Relative risk
SVD	Spontaneous vaginal delivery
UI	Urinary incontinence
UL	Ultrasound examination

Abbreviations used in tables are described in table text.

Definitions used in the thesis

The definitions of UI were updated in 2010 in the Report from the standardization sub-committee of the International Continence Society and International Urogynecology Association [Haylen 2010].

- Urinary incontinence: the complaint of any involuntary leakage of urine.
- Stress urinary incontinence: the complaint of any involuntary leakage of urine on effort or exertion or sneezing or coughing.
- Urgency urinary incontinence: the complaint of any involuntary leakage of urine accompanied by or immediately proceeded by urgency.
- Mixed urinary incontinence: the complaint of any involuntary leakage of urine associated with urgency and also with effort or exertion or sneezing or coughing.

Incident UI is defined as cumulative incidence of any UI during a certain time periode. Incident stress, urge or mixed UI is defined as new onset of either stress, urge or mixed UI during a certain time period.

The definitions of BMI are based on WHO's definitions of underweight, normal weight and overweight.

- BMI weight (kg) / (height in meters)^2
- Underweight BMI < 18,5 kg/m^2
- Normal weight BMI 18,5 – 24,9 kg/m^2
- Overweight BMI ≥ 25 kg/m^2

The definitions of obstetric variables in MBRN are based on Clinical guidelines in obstetric, 1999, written by The Norwegian society of obstetrics and gynecology [Dalaker K 1999].

- Elective CS: A planned CS usually performed 1-2 weeks due to term.
- Non – elective/acute CS: Emergency CS due to complications in mother or child.
- Vaginal delivery: Represents SVD, forceps delivery or vacuum delivery.
- Apgar score: Number arrived at by scoring the heart rate, respiratory effort, muscle tone, skin colour, and response to a catheter in the nostril. Each of these objective signs can receive 0, 1, or 2 points.
- Fetal presentation: Normal occipital, breech, transverse, abnormal fetal head presentation or other.
- Perineal tear grade 3: Fourchette, perineal skin, vaginal mucosa, muscles, and anal sphincter are torn.
- Perineal tear grade 4: Fourchette, perineal skin, vaginal mucosa, muscles, anal sphincter and rectal mucosa are torn.

General definitions on parity:

- Nulliparous: A woman who is pregnant with her first child.
- Primiparous: A woman who has delivered her first child.
- Parous: A woman who has delivered a child.
- Multiparous: A woman who has delivered more than one child.

Abstract

Urinary incontinence (UI) is a common condition among women. The prevalence of UI is high both during and after pregnancy, and childbearing is an established risk factor for UI among young and middle-aged women. However, incidence and prevalence estimates of UI in association with pregnancy vary widely. Only a few population based studies have investigated prevalence of UI in pregnancy by type and severity. Data are inconsistent regarding several risk factors for UI in pregnancy.

UI starting before or in pregnancy is likely to predict UI postpartum. The role of incident UI in pregnancy has received little attention as a predictor for UI postpartum and later in life. Few authors have studied the effect of delivery mode on UI among primiparous women. Weight gain in pregnancy is thought to contribute to the increased prevalence of UI during and after pregnancy, but scientific support is lacking. The effect of weight loss on UI postpartum is unclear.

The data collection for the current study was conducted as part of the Norwegian Mother and Child Cohort Study (MoBa) at the Norwegian Institute of Public Health. From 1999 to 2009, investigators in MoBa invited all pregnant women in Norway to participate in the study 2 weeks before the routine pregnancy ultrasound examination, aiming at a study population of 100,000 pregnant women. Our sub studies are based on available data at the time from this study population. The MoBa study was comprehensive, obtaining data by questionnaires of 14–18 pages length at seven time points from week 15 in pregnancy to 7 years after birth. We used questionnaire data from Questionnaire 1 received in week 15 of pregnancy, Questionnaire 3 received in week 30 and Questionnaire 4 received six months postpartum.

In **Paper I** we used data obtained from 43,279 women who had answered Questionnaire 3. The study showed that the prevalence of UI increased from 26% before pregnancy to 58% in week 30. The corresponding figures for

nulliparous women were 15% and 48%, and for parous women 35% and 67%. The cumulative incidence was 46%. Stress UI was the most common type of UI in week 30 of pregnancy. Before and in pregnancy the majority of pregnant women leaked less than once per week and droplets only. Parity was a strong and significant risk factor for UI in adjusted analyses both before pregnancy (OR 3.3, 95% CI 3.1–3.5) and in pregnancy (OR 2.1, 95% CI 2.0 –2.2) among parous women compared to nulliparous women. Increasing age and BMI were weaker, but still statistically significant, risk factors.

In **Paper II** we selected nulliparous women who were continent before pregnancy and who had answered Questionnaire 1, 3 and 4 from the above dataset; at total of 12,679 women. Results were stratified for mode of delivery and continence status in pregnancy. UI was reported by 31% of the women 6 months after delivery. Compared with women who were continent in pregnancy, UI was more prevalent 6 months after delivery among women who were incontinent in pregnancy (adjusted RR 2.3, 95% CI 2.2–2.4). Adjusted RR for UI after SVD compared with elective CS was 3.2 (95% CI 2.2–4.7) among women who were continent and 2.9 (95% CI 2.3–3.4) among women who were incontinent in pregnancy.

In **Paper III** we used the same dataset as in **Paper II**. We found that weight gain > 50th percentile during weeks 0–15 of pregnancy was weakly associated with higher incidence of UI at week 30 compared with weight gain ≤ 50th percentile. Weight gain > 50th percentile in pregnancy was not associated with increased prevalence of UI 6 months postpartum. Weight gain > 50th percentile from the start of pregnancy to 6 months postpartum was more strongly associated with having UI 6 months postpartum than was high weight gain in any single sub period. Each kilogram of weight gain in this time period increased the RR for UI by 2.3% (RR 1.02, 95% CI 1.02–1.03). From delivery to 6 months postpartum, there was a clear association between weight loss and lower prevalence of UI among women who were continent and as well as those among those who were incontinent in pregnancy. For each kilogram of

weight loss among all women who were incontinent in pregnancy, the relative risk for UI decreased by 2.1% (RR 0.98, 95% CI 0.97-0.99).

Main findings in the thesis:

- The prevalence of UI was high before pregnancy. Prevalence increased substantially in pregnancy and was reduced postpartum. Prevalence of UI postpartum was, however, higher than before pregnancy.
- UI in pregnancy was associated with UI postpartum. Vaginal delivery was a strong independent risk factor for UI postpartum.
- The association between UI postpartum and mode of delivery was not significantly influenced by incontinence status in pregnancy. Prediction of a group with high risk of incontinence postpartum by mode of delivery cannot be based on continence status in pregnancy.
- Weight gain in the beginning of pregnancy was weakly associated with UI in pregnancy. The association is not likely to be of clinical importance as the weight gain in beginning of pregnancy was not associated with UI postpartum. Weight loss postpartum seemed to have an impact in avoiding UI and regaining continence 6 months postpartum.

Sammendrag (abstract in Norwegian)

Urininkontinens (UI) er en vanlig tilstand blant kvinner. Prevalensen av UI er høy både under og etter svangerskapet. Graviditet er en etablert risikofaktor for UI blant yngre og middelaldrende kvinner. Imidlertid varierer insidens og prevalensestimatene for UI i forbindelse med svangerskap betydelig. Få populasjonsbaserte studier har undersøkt type og alvorlighet av UI under svangerskapet. Det er også sprikende resultater angående risikofaktorer for UI.

UI som oppstår før eller under svangerskapet kan sannsynligvis predikere UI etter fødsel. UI. Nyoppstått UI under svangerskapet har foreløpig fått lite oppmerksomhet som prediktor UI etter fødsel. Få forskere har undersøkt effekten av forløsningsmetode på UI hos førstegangsfødende kvinner. Man har lenge trodd at vektøkning under svangerskapet i betydelig grad har bidratt til den økte UI under svangerskapet, men vitenskapelig dokumentasjon mangler. Effekten av vekttap etter fødsel på UI etter fødsel er uklar.

Datainnsamlingen for denne studien ble gjennomført av Den Norske Mor og Barn Undersøkelsen (MoBa) ved Folkehelseinstituttet. Fra 1999 til 2009 ble alle gravide norske kvinner invitert til å delta i studiet 2 uker før rutine ultralydsundersøkelse. Målet var å rekruttere 100,000 gravide kvinner. Våre substudier baserte seg på daværende tilgjengelige data fra MoBa studien. MoBa studien var omfattende med innsamling av 14 – 18 siders spørreskjema ved syv anledninger fra uke 15 i svangerskapet til 7 år etter fødsel. Vi benyttet data fra spørreskjema som ble utsendt i uke 15 (spørreskjema 1) og 30 (spørreskjema 3) av svangerskapet og 6 måneder etter fødsel (spørreskjema 4).

I Artikkel I benyttet vi data fra 43,279 som hadde besvart spørreskjema 1 og 3. Studien viste at hyppigheten av UI økte fra 26 % før svangerskapet til 58 % i uke 30. Tallene for førstegangsfødende var 15 % og 48 %, for flergangsfødende 35 % og 67 %. Nyoppstått UI forekom hos 46 %. Stress UI

var den vanligste formen for UI i uke 30. Under og etter svangerskapet hadde majoriteten av gravide kvinner lekkasje sjeldnere enn 1/uke og kun noen dråper. Tidligere fødsler var en sterk og signifikant risikofaktor for UI i justerte analyser både før svangerskap (OR 3.3 95 % CI 3.1–3.5) og under svangerskap (OR 2.1 95 % CI 2.0–2.2) blant flergangsgravide kvinner sammenlignet med førstegangsgravide kvinner. Alder og kroppsmasseindex var svakere, men fortsatt statistisk signifikante risikofaktorer.

I Artikkel II selekterte vi førstegangsfødende kvinner som var kontinente før svangerskapet og som hadde besvart spørreskjema 1, 3 og 4 fra MoBa; totalt 12,679 kvinner. Resultatene ble stratifisert for forløsningsmetode og kontinensstatus under svangerskapet. UI ble rapportert av 31 % av kvinnene 6 måneder etter fødsel. UI mer prevalent 6 måneder etter fødsel blant kvinner som var inkontinent under svangerskapet (OR 2.3 95 % CI 2.2–2.4) sammenlignet med kvinner som var kontinente under svangerskapet. Justert RR for UI etter spontan vaginal forløsning sammenlignet med keisersnitt var 3.2 (95 % CI 2.2–4.7) blant kvinner som var kontinente og 2.9 (95 % CI 2.3–3.4) blant kvinner som var inkontinente under svangerskapet.

I Artikkel III benyttet vi samme datasett som i Artikkel II. Vi fant at vektøkning > 50 prosentilen i uke 0 – 15 i svangerskapet var svakt assosiert med høyere innsidens av UI i uke 30 av svangerskapet sammenlignet med vektøkning ≤ 50 prosentilen. Vektøkning > 50 prosentilen under svangerskapet var ikke assosiert med økt hyppighet av UI 6 måneder etter fødsel. Vektoppgang > 50 prosentilen fra begynnelsen av svangerskapet til 6 måneder etter fødsel var sterkere assosiert med UI enn vektoppgang i noen annen tidsperiode. For hvert kg vektøkning økte RR for UI med 2.3 % (RR 1.02; 95 % CI 1.02–1.03). Fra fødsel til 6 måneder etter fødsel var det en klar assosiasjon mellom vekttap og lavere prevalens av UI både blant kvinner som var kontinent og blant kvinner som var inkontinent under svangerskapet. For hvert kg vektreduksjon blant kvinner som var inkontinent under svangerskapet sank RR for UI 2.1 % (RR 0.98 95 % CI 0.97–0.99).

Hovedfunn i denne avhandlingen:

- Prevalensen av UI var høy før svangerskapet. Prevalensen økte betydelig under svangerskapet og ble redusert etter fødsel. Prevalensen etter fødsel var imidlertid høyere enn før svangerskapet.

- UI under svangerskapet var assosiert med UI etter fødsel. Vaginal forløsning var en sterk uavhengig risikofaktor for UI etter fødsel.

- Assosiasjonen mellom UI etter fødsel og forløsningsmetode ble ikke signifikant påvirket av kontinentsstatus under svangerskapet. Prediksjon av en gruppe kvinner med høy risiko for UI etter fødsel på bakgrunn av forløsningsmetode kunne ikke baseres på kontinentsstatus under svangerskapet.

- Vektøkning i begynnelsen av svangerskapet var svakt assosiert med UI under svangerskapet, men assosiasjonen er trolig ikke klinisk betydningsfull da vektøkning under svangerskapet totalt sett kke var assosiert med UI etter fødsel. Vekttap etter fødsel så ut til å være viktig for å unngå UI og gjenvinne kontinens 6 måneder etter fødsel.

List of publications

This thesis is based on the following three articles.

I. Wesnes SL, Rortveit G, Bo K, Hunskaar S. 2007. Urinary incontinence in pregnancy. Obstet Gynecol 109: 922 – 928.

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II. Wesnes SL, Hunskaar S, Bo K, Rortveit G. 2009. The effect of urinary incontinence status during pregnancy and delivery mode on incontinence postpartum. A cohort study. BJOG 116: 700 – 707.

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III. Wesnes SL, Hunskaar S, Bo K, Rortveit G. 2010. Urinary incontinence and weight gain in pregnancy: a cohort study. Am J Epidemiol 172: 1034 – 1044.

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The respective articles are referred to as **Paper I**, **Paper II** and **Paper III** in the thesis.

1. Introduction

This introduction will present background information about incidence, prevalence and risk factors for UI in pregnancy and postpartum. In addition, the introduction will discuss aspects on the association between UI and weight that are beyond weight change in pregnancy.

I will not refer to **Paper I**, **Paper II** or **Paper III** in the introduction, as these papers will be thoroughly discussed in the Discussion section.

1.1 Incidence and prevalence of UI in pregnancy

Incidence

UI is common among nulliparous women. A Norwegian study found prevalence of UI among nulliparous women aged 20 – 34 and 35 – 44 to be 8 % and 15 %, respectively [Rortveit 2001]. Other studies have found that 11 % [Brown 2010, MacLennan 2000] of nulliparous women had UI before pregnancy. Prevalence of UI increases considerably in pregnancy due to increased incidence of stress and mixed UI [Solans-Domenech 2010].

No systematic review has presented pooled incidence of UI in pregnancy. Epidemiologic data are somewhat scarce and differ substantially for cumulative incidence of UI in pregnancy; from 8 – 57 % in different studies (Table 1).

Incidence of UI is low in 1. trimester, rising rapidly in 2. trimester and continues to rise, though more slowly, in 3. trimester [Marshall 1998, Morkved 1999, Solans-Domenech 2010]. A large Spanish cohort study from 2010 consisting of 1,128 nulliparous women who were continent before pregnancy had questionnaire data from each trimester. Sandvik's severity index and short version of the International Consultation on Incontinence questionnaire were

used. The article reported a cumulative incidence of UI in pregnancy of 39 % [Solans-Domenech 2010]. An Australian cohort study from 2009 consisting of 1,507 primiparous women had interview data from early and late pregnancy. Sandvik's severity index and an incontinence screening questionnaire for female primary care were used. The authors found an incidence of any UI of 45 % in pregnancy [Brown 2010] (Table 1). These cohort studies have several similarities with our study.

There are a few Scandinavian studies on incident UI in pregnancy. Authors of a Norwegian cross sectional study published data on incidence of UI in pregnancy based on interview and objective testing 8 weeks postpartum. They found an incidence of 38 % of UI in pregnancy [Morkved 1999]. Authors of a Swedish cohort study followed pregnant women from week 12 to 36. By repeated measurements they found an incidence of stress UI of 16 % in week 36 [Kristiansson 2001]. A Danish cross sectional retrospective study found an incidence of UI of 17 % in pregnancy [Hvidman 2002]. By interview and examination a 30 years old large Swedish cohort study on incident stress UI in pregnancy reported that 16 % of women experience stress UI for the first time in pregnancy [Iosif 1981] (Table 1).

Several studies on incident UI in pregnancy are cross sectional. Some obtained data on any UI while others had data on stress UI only, some use questionnaire data while others use interview and objective testing. This might explain the diverging estimates (Table 1). The MoBa study can help us estimate incidence of UI in pregnancy.

Table 1. Incidence of urinary incontinence in pregnancy by parity.

Authors, year	Origin	Design	N	Time of UI	Type of data collection	Nulliparous	Parous
[Al-Mehaisen 2009]	Jordan	Cohort	181	3. trimester	Interview .	45 %	54 %
[Arrue 2010]	Spain	Cohort	396	Delivery	Ex., interview	31 %	
[Brown 2010]	Australia	Cohort	1,507	3. trimester	Questionnaire, interv.	45 %	
[Chiarelli 1997]	New - Zealand	Cross-s	304	During pregn.	Interview		57 %
[Dimpfl 1992]	Germany	Cross-s	180	During pregn.	Interview		54 %
[Glazener 2006]	UK, N.Z.	Cross-s	3,405	During pregn.	Questionnaire	11 %	
[Groutz 1999]	Israel	Cross-s	300	3 days PP	Interview	28 %	49-50 %
[Hvidman 2002]	Denmark	Cross-s	642		Questionnaire	17 %	8 %
[Iosif 1981]	Sweden	Cohort	1,411	1-2 weeks PP	Ex, interview		16 % (s)
[Kristiansson 2001]	Sweden	Cohort	200	3. trimester	Questionnaire		14 % (s)
[Morkved 1999]	Norway	Cross-s	144	During pregn.	Ex., interv.		38 % (s)
[Sharma 2009]	India	Cohort	240	3. trimester	Questionnaire		18 %
[Solans-Domenech 2010]	Spain	Cohort	1,128	During pregn.	Questionnaire	39 %	
[Thomason 2007]	USA	Cross-s	121	During pregn.	Ex., interview	16 %	
[Viktrup 1992]	Denmark	Cohort	305	3 mth.	Interview	10 % (s)	

cross-s = cross sectional study, Quest. = Questionnaire, Interv- = interview, Ex. = examination, PP = postpartum, (s) = stress UI

Prevalence

I have not been able to find any systematic review presenting pooled prevalence of UI in pregnancy. The ICI report describes period prevalence of any UI in pregnancy of 32 – 64% among all women [Milsom 2009]. Prevalence estimates for UI in pregnancy among nulliparous women vary from 4 – 70 %, while estimates for parous women vary from 14 – 85 % (Table 2).

Dolan et al investigated prevalence of any UI during week 32 to term in a cohort of 492 nulliparous women in England [Dolan 2004]. The Kings Health Questionnaire was used to assess any UI. Prevalence of UI was 36 % in pregnancy. However, prevalence of UI before pregnancy was only 2.6 %, which might explain a somewhat low UI prevalence during pregnancy. An Australian cohort study consisting of 1,507 nulliparous women found prevalence of any UI of 56 % in week 31 of pregnancy [Brown 2010] (Table 2).

Of several Scandinavian studies presenting prevalence of UI in pregnancy, only 3 were cohorts (Table 2). Iosif et al interviewed and examined 1,411 pregnant women in a Swedish cohort. They found that 22 % of all pregnant women experienced stress UI in pregnancy [Iosif 1981]. Another Swedish cohort study of 200 nulliparous women found by questionnaire a prevalence of stress UI in pregnancy of 26 % among all women [Kristiansson 2001]. In a Danish cohort 305 primiparous women were interview in pregnancy regarding UI. 32 % of the women experienced stress UI in pregnancy [Viktrup 1992]. A Norwegian retrospective cross sectional study found prevalence of UI in pregnancy to be 37 – 70 %, depending of parity [Morkved 1999].

There are large differences in estimates of UI in pregnancy. Few Scandinavian pregnancy cohorts on UI have been performed, and authors of these cohorts reported data on stress UI only. A new large prospective cohort on pregnant women, like the MoBa, will get new valid data on any UI in pregnancy.

Table 2. Prevalence of urinary incontinence in pregnancy by parity.

Author, year	Origin	Design	N	Time of UI	Type of data collection	Nulliparous	Parous
[Milsom 2009]		Report					32 – 64 %
[Bo 2007]	Norway	Cross-s	40	During pregn.	Questionnaire		19 % (s)
[Burgio 2003]	USA	Cohort	523	2 days PP	Interview		60 %
[Brown 2010]	Australia	Cohort	1,507	3. trimester	Quest, interv	56 %	
[Dimpfl 1992]	Germany	Cross-s	350	During pregn.	Interview		55 %
[Dolan 2004]	UK	Cohort	492	3. trimester	Questionnaire	36 %	
[Francis 1960]	England	Cohort	400	During pregn.	Ex, interview	53 %	85 %
[Groutz 1999]	Israel	Cross-s	300	3 days PP	Interview	49 %	50 %
[Hojberg 1999]	Denmark	Cross-s	7,795	2. trimester	Questionnaire	4 %	14 – 16 %
[Hvidman 2003]	Denmark	Cross-s	376		Questionnaire		18 %
[Hvidman 2002]	Denmark	Cross-s	642		Questionnaire	20 %	24 %
[Iosif 1981]	Sweden	Cohort	1,411	1-2 weeks PP	Questionnaire		22 % (s)
[Kristiansson 2001]	Sweden	Cohort	200	3. trimester	Questionnaire		26 % (s)
[Mason 1999]	England	Cohort	717	3. trimester	Questionnaire	32 %	59 %
[Morkved 1999]	Norway	Cross-s	144	8 weeks PP	Ex., interview	35 %	37 – 70 %
[Raza-Khan 2006]	USA	Cohort	113	3. trimester	Questionnaire	70 %	75 %
[Scarpa 2006]	Brasil	Cross-s	340	3. trimester	Interview	46 % (s)	55 – 64 %
[Thomason 2007]	USA	Cross-s	121	During pregn.	Ex., interview	55 %	
[van Brummen 2006b]	Netherland	Cohort	515	2. trimester	Questionnaire	42 % (s)	
[Viktrup 1992]	Denmark	Cohort	305	During pregn.	Interview	32 % (s)	

cross-s = cross sectional study, Ex. = examination, PP = postpartum, (s) = stress UI

1.2 Incidence and prevalence of UI postpartum

Incidence

Prevalence of UI postpartum is a so called “mixed bag” of incident UI before pregnancy, incident UI in pregnancy and incident UI postpartum [Iosif 1981, Nygaard 2006]. Risk factors for incident UI at the different time points vary. Among several risk factors, pregnancy itself is a risk factor for UI in pregnancy. Mode of delivery is a risk factor for UI postpartum [Glazener 2006].

No systematic review on incident UI postpartum has been identified. In a review on the association between CS on UI postpartum Nygaard reported the range of incident UI postpartum to be 7 – 15 % among all women [Nygaard 2006]. The reported incidence of UI among primiparous and parous women postpartum varies between 0 – 26 % and 4 – 21 %, respectively (Table 3).

A prospective cohort had data on incident UI 6 months postpartum; among 595 primiparous Canadian women 6 months postpartum, Farrell et al found by validated questionnaire an incidence of any UI of 26 % [Farrell 2001] (Table 3). The use of a research nurse to clarify and complete the questionnaire with each participant might explain the high incidence.

Two Scandinavian cohort studies have reported incidence of UI postpartum; in the Swedish cohort of 1,411 primiparous women, 19 % reported incident stress UI 6 months post partum [Iosif 1981]. In the Danish cohort of 305 primiparous women Viktrup et al found an incidence of stress UI of 7 % 3 months after vaginal delivery [Viktrup 1992] (Table 3).

Figures of incident UI post partum varies a lot. Scandinavian cohorts on UI postpartum are 20 – 30 years old. Definitions and statistical methods have changed and developed. There is need for a new large cohort like the MoBa study on UI postpartum.

Table 3. Incidence of urinary incontinence postpartum by parity.

	Origin	Design	N	Type of data collection	Time of UI PP	Primiparous	Parous
[Boyles 2009]	USA	Cross-s	5,599	Questionnaire	6 mth	10 %	
[Burgio 2003]	USA	Cohort	523	Interview	3 mth		10 %
[Chaliha 1999].	England	Cohort	549	Interview	3 mth	6 %	
[Dimpfl 1992]	Germany	Cross-s	350	Interview	3 mth	4 % (s)	4 %
[Farrell 2001]	Canada	Cohort	595	Questionnaire	6 mth	26 %	
[Foldspang 2004].	Denmark	Cross-s	1,232	Questionnaire	> 12 mth		14 %
[Francis 1960]	England	Cohort	400	Ex., interview	3 mth	0 %	
[Glazener 2006]	UK, N.Z.	Cross-s	3,405	Questionnaire	3 mth	15 %	
[Hvidman 2003]	Denmark	Cross-s	642	Questionnaire	3 mth		8 %
[Iosif 1981]	Sweden	Cohort	1,411	Questionnaire	6-12 mth		19 % (s)
[Mason 1999]	England	Cohort	717	Questionnaire	3 mth		15 %
[Morkved 1999]	Norway	Cross-s	144	Ex., interview	2 mth		19 %
[Raza-Khan 2006]	USA	Cohort	113	Questionnaire	Postpartum		4 %
[Solans-Domenech 2010]	Spain	Cohort	1,128	Questionnaire	2 mth	5 %	
[Thomason 2007]	USA	Cross-s	121	Ex., interview	6 mth	16 %	
[Stanton 1980]	UK	Cohort	189	Interview	Postnatally	6% (s), 9% (u)	11% (s), 7% (u)
[Viktrup 1992]	Denmark	Cohort	305	Interview	3 mth	7% (s), 4% (u)	
[Wilson 1996].	New Zealand	Cross-s	1,505	Questionnaire	3 mth	12 %	21 %

cross-s = cross sectional study, Ex. = examination, PP = postpartum, (s) = stress UI, (u) = urge UI

Prevalence

Several reviews present prevalence of UI postpartum. In a review on UI and its precipitating factors postpartum Herbruck reported prevalences of stress UI of 22 – 33 % postpartum among all women [Herbruck 2008]. The ICI epidemiology report presented prevalence of 15–30 % among all women the 1. year postpartum [Milsom 2009]. In a review Nygaard reported the prevalence of UI postpartum to be 9 – 31 % among all women [Nygaard 2006]. Authors of a systematic review reported a pooled prevalence of UI of 29 % and 33 % 3 months postpartum among primiparous and parous women, respectively [Thom 2010] (Table 4). The range of prevalence among primiparous women (6–67 %) and parous women (3–45 %) are, however, wider than the impression given in rewievs (Table 4).

Several studies have presented data on the long term prognoses of UI postpartum. Farrell found that prevalence of UI did not change from 6 weeks postpartum to 6 months postpartum [Farrell 2001]. A systematic review found only small changes in prevalence of UI over the first year postpartum [Thom 2010]. A 12 year prospective study indicates that onset of UI in pregnancy or postpartum increased the risk for UI 12 years later [Viktrup 2006]. As prevalence figures of UI postpartum appear to be stable, time point of data collection postpartum may be of less importance.

A large cohort study on 2,390 Swedish women recruited in pregnancy assessed stress UI at 2 and 12 months postpartum by questionnaire [Schytt 2004]. UI was defined as any UI last week. Data was linked to the Swedish birth registry. The authors found that 18 % of primiparous women and 24 % of multiparous women had stress UI 12 months postpartum. In the Danish cohort from 1992 Viktrup et al found prevalence of stress UI 3 months postpartum to be 7 % among 305 primiparous women [Viktrup 1992]. There are large differences in estimates of UI postpartum (Table 4). A large national cohort on pregnant women like MoBa is desirable, as it would be the first of its kind.

Table 4. Prevalence of urinary incontinence postpartum by parity.

	Origin	Design	N	Ype of data collection	Time of UI PP	Primiparous	Parous
[Altman 2006]	Sweden	Cohort	304	Questionnaire	5 mth	15 % (s)	
[Arrue 2010]	Spain	Cohort	396	Ex., interview	6 mth	15 %	
[Baydock 2009]	Canada	Cross-s	632	Interview	4 mth		23 %
[Bo 2007]	Norway	Cross-s	40	Questionnaire	6 weeks		29 %(s)
[Boyles 2009]	USA	Cross-s	5,599	Questionnaire	6 mth	26 %	
[Burgio 2003]	USA	Cohort	523	Interview	6 mth		11 %
[Chaliha 2002]	England	Cohort	161	Questionnaire, urodyn	3 mth	30 %	
[Chaliha 1999].	England	Cohort	549	Interview	3 mth	15 %	
[Dimpfl 1992]	Germany	Cross-s	350	Interview	3 mth	6 % (s)	
[Dolan 2004]	UK	Cohort	492	Questionnaire	3 mth	13 %	
[Eason 2004]	Canada	Cohort	949	Questionnaire	3 mth		31 %
[Ege 2008]	Turkey	Cross-s	1,749	Questionnaire	12 mth		20 %
[Ekstrom 2008]	Sweden	Cohort	389	Questionnaire	3 mth	13% (s), 4% (u)	
[Eliasson 2005]	Sweden	Cohort	665	Questionnaire	12 mth	49 %	
[Ewings 2005]	England	Cohort	723	Questionnaire	6 mth		45 %
[Farrell 2001]	Canada	Cohort	595	Questionnaire	6 mth	26 %	
[Foldspang 2004].	Denmark	Cross-s	1,232	Questionnaire	> 12 mth	26 %	
[Francis 1960]	England	Cohort	400	Ex, interview	3 mth	24 %	29 % (s)

[Glazener 2006]	UK, N.Z.	Cross-s	3,405	Questionnaire	3/ >12 mth	29 % / 38 %	
[Hatem 2005]	Canada	Cross-s	2,492	Questionnaire	6 mth	30 %	
[Hvidman 2003]	Denmark	Cross-s	642	Questionnaire	3 mth		3 %
[Mason 1999]	England	Cohort	717	Questionnaire	3 mth	10 % (s)	31 % (s)
[Meyer 1998]	Switzerland	Cohort	141	Ex., interview	9 weeks		36 %
[Morkved 1999]	Norway	Cross-s	144	Ex., interview	2 mth		38 %
[Pregazzi 2002]	Italy	Cross-s	537	Ex., interview	3 mth	8 %	20 %
[Raza-Khan 2006]	USA	Cohort	113	Questionnaire.	Postpartum	46 %	43 %
[Sampselle 1996]	USA	Cohort	59	Questionnaire., ex.	6 mth	67 % (s)	
[Schytt 2004]	Sweden	Cohort	2,390	Questionnaire	12 mth	18 % (s)	24 % (s)
[Stanton 1980]	UK	Cohort	189	Interview	3 mth	6 % (s), 8 % (u)	
[Thomason 2007]	USA	Cross-s	121	Ex., interview	6 mth	45 %	
[Torrisi 2007]	Italy	Cohort	562	Ex., interview	3 mth		11 % (s)
[Viktrup 1992]	Denmark	Cohort	305	Interview	3 mth	7 % (s)	
[Wijma 2003]	Netherland	Cohort	117	Questionnaire, ex.	6 mth	15 %	
[Wilson 1996].	N.Z	cross-s	1,505	Questionnaire	3 mth	29 %	34 %

cross-s = cross sectional study, Ex. = examination, PP = postpartum, (s) = stress UI, (u) = urge UI, Urodyn = urodynamic testing, mth = months

1.3 Why do estimates differ?

A wide range of prevalence estimates of UI in pregnancy and postpartum have been presented. There are several methodological reasons for these diverging incidence and prevalence estimates.

UI definition

UI can be defined as a:

- symptoms (a morbid phenomenon or departure from the normal in structure, function, or sensation, experienced by the woman and indicative of disease or a health problem) [Abrams 1988, Abrams 2002, Haylen 2010]

- signs (observed by the physician to verify symptoms and quantify them) [Abrams 1988, Abrams 2002, Haylen 2010]

- urodynamic findings (observations made during urodynamic studies) [Abrams 2002]

- conditions (the presence of urodynamic observations associated with characteristic symptoms or signs and/or non-urodynamic evidence of relevant pathological processes) [Abrams 2002]

The ICS definitions and terminologies of UI according to the above descriptions have been revised several times [Abrams 1988, Abrams 2002, Haylen 2010]. The current definition of UI symptoms is “Complaint of involuntary loss of urine” [Haylen 2010]. In the 2002 defintion, UI symptoms were not enough to set the UI diagnose; UI signs were needed. Today the majority of studies on UI define UI according to UI symptoms. Studies on UI have used the definitions at the time. As definitions change, prevalence estimates will also change.

Information gathering

Information on UI in pregnancy and postpartum is often gathered through questionnaires, but objective testing [Morkved 1999], personal structured interviews [Chiarelli 1997, Morkved 1999] or semi structured interviews [Spellacy 2001] or phone interviews [Baydock 2009] by doctors or assistants, or reviews of existing medical records [Spellacy 2001] are also used. Information collected by interview makes it possible to clarify and gather more and better information regarding UI. This type of data collection is likely to lead to higher prevalence figures of UI than for instance questionnaire [Chiarelli 1997]. Medical records often lack important information, leading to low prevalence estimates. Studies have found low agreement between self reported UI and clinical assessment [Diokno 1988, Milsom 1993]. Objective testing according to the “UI sign” definition will lead to lower prevalence estimates than questionnairebased studies using the “UI symptom” definition.

Type of study

A large proportion of studies on UI in pregnancy or postpartum are cross sectional (Table 1 – 4) or retrospective. If a woman has UI when answering a retrospective study, this may affect her reporting of UI by improving her memory about earlier UI leading to a recall bias. Cross sectional studies have less valid incidence figures than prospective cohorts.

Timing of data collection

Timing of data collection can affect prevalence estimates of UI in pregnancy. Some studies question women about UI during each trimester, but most studies question women at one certain time point in pregnancy [Brown 2010, Lewicky-Gaupp 2008] or just after birth [Sottner 2006]. Some studies do not report what time in pregnancy the women reported UI [Sharma 2009]. As prevalence of UI increases in pregnancy, the time of information gathering will affect the prevalence estimates. When it comes to data collection postpartum

some studies report on UI at 6 - 9 weeks postpartum [D'Alfonso 2006, Lewicky-Gaupp 2008, Meyer 1998], 3 months [Eason 2004, Hannah 2002], 4 months [Baydock 2009], 6 months [Thomason 2007], 12 months [Serati 2008] or > 12 months [Foldspang 2004, Fritel 2004] postpartum. The time of information gathering postpartum might affect incidence and prevalence estimates of UI. However, a recent review indicates that prevalence of UI is stable first year postpartum [Thom 2010], and time of data collection postpartum may therefore be of less importance.

Threshold

Permanence, frequency and volume are used by authors as threshold to define women with UI in association with pregnancy. Permanence or duration can be defined as one or more episodes of UI in the previous month [Brown 2010, Wilson 1996]. Some authors use longer periods, like trimesters [Schytt 2004] or the 6 months postpartum period [Schytt 2004]. Some authors investigate severe UI defined by weekly or daily leakage [Al-Mehaisen 2009] while others do not report any cut-off [van Brummen 2006b]. Some studies have a cut-off for minimum frequency, amount or severity of UI for women to be included in the study as incontinent. A high cut-off decreases the number of women who fulfil the UI criteria in a study. Differing thresholds may explain differing incidence and prevalence estimates of UI.

Type of UI

Stress UI is more common in pregnancy and postpartum than urge UI and mixed UI. Also, the incidence of pure urge UI in pregnancy or postpartum is low compared to incidence of stress UI and mixed UI. The prevalence of pure stress UI is reported to be 2 – 8 times higher than the prevalence of pure urge UI in pregnancy [Brown 2010, Goldberg 2005, Raza-Khan 2006]. Prevalence of mixed UI is reported to be 0.3 – 1.5 times of the prevalence of pure stress UI in pregnancy [Brown 2010, Goldberg 2005, Raza-Khan 2006]. The stress/urge ratio is reduced postpartum as prevalence of stress UI decline.

Several studies focus solely on stress UI [Mason 1999, Torrisi 2007, Viktrup 1992]. Prevalence figures in these studies are likely to be lower than in studies that include both urge UI and mixed UI in their analyses.

Charecteristics of study population

The study population influences prevalence of UI. Some studies on UI in association with pregnancy use study populations from tertiary care hospitals [Baydock 2009], leading to recruitment of highly selected participants. BMI distribution, age distribution, parity distribution, proportion of European or Hispanic population, proportion of women having vaginal delivery all influence prevalence figures of UI. Some studies include only women having SVD [Altman 2006, Arrue 2010, Baydock 2009], which will give a higher prevalence estimate of UI than if the study also had included CS. Many studies on UI in association with pregnancy either adjust or report stratified analyses for age [Solans-Domenech 2010], BMI [Eason 2004], race [Connolly 2007] and mode of delivery [Eason 2004]. Effect estimates are therby controlled for baseline imbalances in these important patient characteristics. However, dissimilar use of statistical stratification and adjustment makes it difficult to compare findings. Pooled prevalences figures can be misleading and readers should be careful in generalising the findings to a population outside the study population.

Bias

Many studies on UI in pregnancy try to gather information from all pregnant women in the community [Boyles 2009, Thompson 2002]. In large studies with an open invitation and no follow – up of non – responders to the invitation it can be difficult to achieve high response rates. These studies are prone to a biased response rates/selection bias which may invalidate the prevalence estimates. Primiparous women are more likely to participate and tell their pregnancy stories in studies compared to parous women [Magnus 2006]. Known differences between responders and non-responders may be compensated during analyses. The major problem is unknown response bias,

such as the possibility of different response rates between continent and incontinent women [Cartwright 1983]. Due to embarrassment and feeling uncomfortable about reporting UI, incontinent women may deny or not answer questions about UI. Converely, incontinent women may find the subject particularly relevant, and therefore respond to a greater extent than continent women. At present, we do not know how these factors may affect the response rates. To minimise selection bias one should always aim at the highest possible response rates.

All the above methodological factors can influence UI estimates in a study. Unfortunately we do not know all factors that influence UI estimates. Some variation in prevalence estimates between studies will always remain.

1.4 What is a risk factor?

A risk factor is a variable associated with an increased risk of the outcome. Risk factors imply association and not necessarily causality.

Studies with large study populations are likely to find statistically significant associations. It does not, however, imply that the association is clinically significant; which means that the risk is large enough to be of practical importance to patients and healthcare providers. Assessing clinical significance takes into account factors such as the size of a treatment effect, the severity of the condition being treated, the side effects of the treatment, and the cost.

There are several criteria for causation and risk factors. Hill's Criteria of Causation from 1965 [Hill 1965] and Evan's Postulates from 1976 are some. Several of these criteria are indirectly still being used when we talk about established risk factors. For a risk factor to be defined as "established", "true" or "verified", several items should be achieved:

- The effect size (OR, RR) tells us something about the strength, relevance and clinical importance of the risk factor. Statistical significance and confidence intervals tell us whether the risk factor is random or trustworthy.

- A risk factor does not necessarily imply a cause and effect relationship. To be causal the risk factor must precede the outcome. This is why cross sectional studies provide weaker evidence than cohorts for causal relationships.

- A dose – response relationship strengthens the association. If the OR for a disease increases after increasing exposure for the risk factor, association is likely. If treatment, reduction of risk factor by purpose or by chance reduces the incidence of the outcome, this supports that there is a causal relationship.

- Consistency in the literature regarding a risk factor increases the chance of validity. This implies that the risk factor is reproduced in several studies with different study populations at different times at different places.

- If the risk factor is biologically plausible and supported by biological evidence, it strengthens the possibility of causality. However, many epidemiological studies are prior to biological evidence, and lack of knowledge makes it thereby hard to explain how the risk factor acts on the outcome.

There are proposed several risk factors for UI in general and for UI in pregnancy and post partum. Some of these suggested risk factors are listed in Table 5. Age, BMI, pregnancy, parity and mode of delivery are considered established risk factors, but there are inconsistent findings regarding most of the remaining listed risk factors.

Some findings must be regarded as simple “associations” or “predictors”; for example education and income. In quantitative research, the term "association" is often used to emphasize that a relationship is not necessarily causal. It is difficult to find biological plausible evidence for these associations. Some findings are regarded as “risk factors” like age and SVD, as they meet

Table 5. Varialbles that might increase the risk of UI

General risk factors for UI	Risk factors for UI in association with pregnancy
Increasing age	Pregnancy per se
Increasing BMI	Increasing parity
Low education	Mode of delivery (SVD vs. CS)
Low income	Forceps, vacuum delivery vs SVD
Smoking vs no smoking	Increasing degree of laceration, perineal suturing
Increasing alcohol consumption	Episiotomy vs no episiotomy
Race (white vs. black)	Increasing length of 2. stage labour, increasing total duration of labour
Hereditary factors	Delivery position, fetal head presentation
Increasing exercise	Increasing head circumference
Increasing intake of fatty food	Increasing birth weight
Diabetes	Increasing weight gain in pregnancy
Depression	UI before pregnancy vs no UI before pregnancy
Asthma, COPD	UI in pregnancy vs no UI in pregnancy
Constipation	Pudendal block, epidural analgesia vs no anesthesia
Nocturia	Induction of labour vs no induction
Hormone therapy	Increasing length of breast feeding
Age at menopause	Increasing striae
Degree of pelvic organ prolapse	Increasing age at first childbirth

all the Hill's criteria to be characterised as established causlal risk factors. Some findings can be said to be in the grey zone between a risk factor and an

associated factor. A condition today can hardly be characterised as a risk factor for the same condition tomorrow. If UI is a stable chronic condition, UI in pregnancy can only be a predictor, or associated with UI postpartum. However, if UI during pregnancy and UI postpartum are conditions at separate times due to separate risk factors, they might be regarded as partly independent. In this setting, UI is not a stable condition, and authors therefore often characterise UI in pregnancy as a risk factor for UI postpartum.

Few risk factors for UI in pregnancy and postpartum are well documented and established. There is a need of studies designed to further investigate risk factors associated with UI in pregnancy and postpartum.

1.5 CS to prevent UI

Several studies and reports from high – income [Collins 2001, Kozak 2002] and low – income countries [Behague 2002, Sreevidya 2003] confirm increasing rates of CS. During the last 50 years Norway has had an increase in CS rate; from 1.8 % in 1967, 6.4 % in 1977, 12.8 % in 1997 to 16.7 % in 2007 [MBRN 2010]. Norway has however a low CS rate compared to similar countries. Surveys on both women [Wax 2004] and obstetricians [Al-Mufti 1997] suggest that a significant proportion would choose to have their own baby delivered by CS. The reasons for increasing CS rates are diverging.

Risks involved by undergoing an elective CS should always be kept in mind before CS is performed as UI prophylaxis. Today prophylactic elective CS is promoted to prevent postpartum UI without robust evidence to support this practice [Dietz 2006, Handa 1996, Leijonhufvud 2011]. Some studies indicate that CS reduces risk of UI, but the clinical significance of these findings remains unclear.

1.5.1 Effect of mode of delivery on UI in the short and long run?

Some studies have investigated the effect of CS on UI. A systematic review [Press 2007] identified two *cross sectional* studies [MacLennan 2000, Rortveit

2003a] with data on primiparous women with results on the effect of CS compared to SVD on stress UI postpartum. The review presented pooled prevalences of stress UI after CS (9 %) and SVD (14 %), leading to an OR of 0.59 (95% CI 0.40 – 0.87) [Press 2007]. There were no significant differences between urge UI and mixed UI after CS compared to SVD.

In the EPINCONT study [Rortveit 2003a], a large cross sectional study from Norway including 15,307 women who had only delivered by CS or vaginal delivery, the prevalence of any UI was 16 % among women who had delivered by CS only, and 21 % in women following VD only. In women 50 – 64 years there was no significant risk difference between women delivering by CS or vaginal delivery. The protective effect of CS seems to be apparent until women are 50 years of age. These findings are supported by other studies, indicating that nulliparous and multiparous postmenopausal women have rather similar risk of UI [Buchsbaum 2002]. One study has performed urodynamic investigation among climacteric women [Guarisi 2002]. There was no difference in uroflowmetry parameters among women who had delivered by CS and vaginal delivery.

The same review [Press 2007] presented pooled prevalences of UI postpartum based on data on primiparous women in *cohort studies* [Press 2007]. Five articles were identified [Fritel 2004, Klein 2005, Schytt 2004, Thompson 2002, Wilson 1996]. Pooled prevalence of stress UI after CS compared to SVD (instrumental deliveries were excluded from analyses) was 10 % and 22 %, respectively, leading to an OR of 0.40 (95 % CI 0.29 – 0,54). There were significant differences in urge UI (OR 0.46, 95 % 0.25 – 0.86) and mixed UI (OR 0.23, 95 % CI 0.05 – 0.95) among primiparous women after CS compared to SVD. Pooled prevalences from two cohort studies [Farrell 2001, Hannah 2004] on any UI did not show significant differences between any CS and SVD (0.74, 95 % CI 0.54 – 1.01) [Press 2007]. Also, when only severe UI was investigated there was no significant risk difference between CS and SVD [Press 2007].

Farrell et al [Farrell 2001] studied primiparous women 6 months postpartum in a cohort study. Women delivering by vaginal delivery had significantly higher risk of any UI compared to women delivering by CS (RR 2.8). There is, however, inconsistency in the literature. Groutz et al [Groutz 2004] found no difference in prevalence of any UI when comparing all CS to vaginal delivery. But when comparing elective CS (3.4% UI) to vaginal delivery (10.3 % UI) among primiparous women 1 year postpartum the difference was significant.

In a cohort study, Wilson et al [Wilson 2002] investigated risk of any UI 4 – 7 years postpartum among primiparous women. They found no significant protection against UI after the first CS compared to vaginal delivery, but they found a 15 % reduction of UI after ≥ 2 CS. Results from a recently published 12 year cohort show that risk of UI after 2 CS is significantly reduced compared to SVD even 11 years after last birth. A combination of CS and SVD does not lead to a significantly reduced UI risk compared to SVD [MacArthur 2011]. In the systematic review on cohort studies with a follow up time of > 1 year, the protective affect of CS remained for stress and mixed UI [Press 2007].

The effect of CS and SVD on prevalence of UI during a short and long time period is rather clear, but the clinical significance is still unclear. Current evidence does not support routine use of elective CS to prevent UI. Several studies on UI and mode of delivery are not primarily designed or powered to explore this issue. Lack of focus on timing of CS, influence of instrumental delivery, adjustments for age and parity are some of the factors affecting the results. There is still need for new prospective cohorts to investigate the effect of mode of delivery on UI and take time point, phase of birth, planned or not planmed CS into account, and to clarify whether certain conditions or groups are more prone to the protective effect of CS on UI postpartum.

1.5.2 Why less UI after CS compared to SVD?

Vaginal delivery is the physiological mode of delivery. Despite this, it may be associated with significant short and long term complications. During delivery, prolonged pressure from the baby's head on the pelvic floor may cause neuropraxia. The nervous pudendus is particular vulnerable to damage. As the baby passes through the vaginal canal, a variety of traumas to muscles, fascias and connective tissues affect the pelvic floor and urethral support, which are all associated with UI [Handa 1996]. Damage to the pelvic floor might occur after the distention during the active second stage of labor [Chaliha 2009], and damage increases with prolonged second stage of labor, episiotomy, forceps delivery, and increased fetal size [Wax 2004]. Women with elective CS will not experience these injuries.

One ultrasound study found a larger levator hiatus area and increased bladder neck mobility among women with vaginal delivery compared to CS [Toozs-Hobson 2008]. In another study researchers used ultrasound and cotton swab test to assess urethral profilometry and vesical neck mobility. Incident UI after the first SVD was associated with lower maximal urethral closure pressure and vesical neck mobility [DeLancey 2007]

Deindl et al found that electromyography of the muscle activity in the pelvis was similar in continent nulliparous women and incontinent parous women with the exception of asymmetric and uncoordinated activity pattern in the levator muscle among parous incontinent women, which affects the continence mechanisms [Deindl 1994]. Concentric electromyography and pudendal nerve conduction studies have found an association between degree of denervation injuries and multiparity, fetal head size, forceps and long second stage of delivery [Allen 1990, Snooks 1984].

A cohort study examined 200 nulliparous women in pregnancy and postpartum [Dietz 2005]. By flowmetry, ultrasound of residual urine and bladder neck mobility the authors found that voided volume decreased in pregnancy and

increased again postpartum. Maximum flow rate increased in pregnancy and continued to increase postpartum. These findings correlated significantly with changes in several parameters of bladder neck mobility. There were, however, no significant differences postpartum among women who delivered by CS or SVD. Several other studies have also not been able to confirm urodynamic differences between women delivering by vaginal delivery or CS [Chaliha 2002, Guarisi 2002, Leijonhufvud 2011].

1.6 Incident UI in pregnancy as a risk factor for UI postpartum

UI postpartum can start before pregnancy, or occur for the first time in pregnancy or after delivery. Accroding to one study, about 65 % of all women with UI during their life will recall that their UI started up either in pregnancy or postpartum [Handa 1996]. Women with UI before pregnancy are nearly 3 times more likely to have UI postpartum [Farrell 2001].

UI in pregnancy appears to be associated with UI postpartum (Se also 1.4: What is a risk factor?). Few studies have investigated this association (Table 6). When reanalyzing available data on primiparous women who were continent before pregnancy in previously published articles, ORs for UI postpartum among women who were incontinent in pregnancy compared to women who were continent in pregnancy vary from 1.7 to 7.8 during the 3 – 12 month postpartum period (Table 6). In adjusted analyses on primiparous women, Dietz-Itza found incident stress UI in pregnancy to be the only independent predictor of stress UI 12 months postpartum [Diez-Itza 2010]. A study from USA enrolled primiparous women 6 – 9 months postpartum. The women were continent before pregnancy and had delivered by vaginal delivery [Thomason 2007]. The authors found, based on retrospective data, that 78 % of women who had UI 6 – 9 months postpartum leaked also in pregnancy.

Table 6. UI in pregnancy as a risk factor for UI postpartum.

Source	Country	Design	Participants	UI status before pregnancy	No. primiparous	Time point	UI %	Association with pp UI.	Confounder control
[Arrue 2010]	Spain	Prospective	Primipara	Continent	396	6 months	15 %	OR 3.7	Y
[Diez-Itza 2010]	Spain	Prospective	Primipara	Continent	352	12 months	11%	OR 5.8	N
[Glazener 2006]	New Zeal, Scotland, England	Rertro/prospective	Primipara	Continent	3,276	3 months	28%	OR 1.7	N
[Groutz 2004]	Israel	Prospective	Primipara	Continent	245	12 months		OR 7.8 $ ^	N
[Viktrup 1992]	Denmark	Prospective	Primipara	Continent	291	3 months		OR 1.9 $ ^	N
[Wilson 1996]	New Zeal.	Retrospective	Primipara	Continent	587	3 months	21%	OR 2.0 $	N
[Foldspang 2004]	Denmark	Retrospective	Primipara	Mixed	1,232	>12 months	67%	OR 8.6	N
[Fritel 2004]	France	Retrospective	Primipara	Mixed	307	48 months	40%	OR 2.5 ^	
[Schytt 2004]	Sweden	Prospective	Primipara	Mixed	1,051	12 months	31%	RR 2.1 ^ #	
[van Brummen 2007]	Netherland	Prospective	Primipara	Mixed	524	12 months		OR 5.5 ^	Y

^ Stress UI only
# Not statistical significant in multivariate analyses.
$ Estimated from numbers in article.

Many authors have found that UI in pregnancy is an important predictor for UI also later in life [Altman 2006, Burgio 2003, Diez-Itza 2010, Foldspang 2004, Hvidman 2003, Schytt 2004, van Brummen 2007, Viktrup 2006]. Viktrup questioned a total of 278 primiparous women about lower urinary tract symptoms after their first pregnancy, and again 12 years later [Viktrup 2006]. Stress UI during the first pregnancy and postpartum period predicted an increased risk of having UI 12 years later. Foldspang found that 56 % of all cases of any UI 1 – 10 years postpartum could be attributed to incident UI in pregnancy [Foldspang 2004].

It appears to be an association between (incident) UI in pregnancy and UI postpartum and later in life. Both the estimates and study designs vary a lot. Large prospective cohorts may investigate the association between incident UI in pregnancy and UI postpartum, and to further search for obstetric factors and treatment that might lower the associated risk.

1.6.1 Why does incident UI in pregnancy persist?

Causative mechanisms for incident UI after labour differ from UI that arise during pregnancy. Several attempts have been made to explain the associations between incident UI during birth and UI postpartum: duration of second stage of labour, episiotomy, vacuum and forceps delivery and increased fetal size. However, we know that women who have only delivered by CS still have a higher prevalence of UI than nulliparous women [Rortveit 2003a]. There must be factors in pregnancy, apart from risk factors in association with delivery, which influence UI postpartum.

Several theories can be put forward to explain the association between UI in pregnancy and UI postpartum:

- UI that is incident in pregnancy (not in association with labour) might be due to stretching and distending of the pelvic floor in late pregnancy; resulting in functional and anatomical alteration in muscles, nerves and connective tissue.

If these effects lead to UI, and the pelvic injuries are not healed postpartum, UI is likely to persist. The mechanisms of connective tissue injury and repair in the pelvis are, however, poorly understood.

- UI in pregnancy could be a sign of congenital poor quality of the connective tissue supporting the urethra and the bladder neck. Some women may have an inherent risk of UI that leads to UI in pregnancy.

- It is known that collagen metabolism is modified in individuals with stress UI. Joint laxity increases in pregnancy, but it is unknown if it subsequently returns to pre-pregnancy levels [Schauberger 1996]. Researchers have found association between relaxin levels in pregnancy and UI postpartum [Tincello 2003]. However, no association have been found between markers of collagen weakness (stria and joint hyper mobility) and risk of UI [Braekken 2009, Chaliha 1999].

- Bladder neck hypermobility is associated with stress UI. Bladder neck hypermobility increases in pregnancy, and this is found to correlate with a significantly increased risk of postpartum UI [Dietz 2005]. Bladder neck hypermobility is further associated with SVD and instrumental vaginal delivery [Dietz 2005]; also this correlates with increased prevalence of UI postpartum. Pregnancy might be the last straw that leads to UI among women with potential bladder neck hypermobility

Our insight into causal mechanisms for UI in pregnancy is still limited. It is therefore also difficult to explain the mechanisms behind persistent UI postpartum. The answer to why incident UI in pregnancy persists after birth is unclear.

1.7 The effect of UI status in pregnancy and mode of delivery on UI postpartum

There is some confusion among health personnel about advocating elective CS to prevent UI [Groutz 2004, Handa 1996, Heit 2001]. There have been several innuendoes about which women that will benefit the most from CS.

We know that prevalence of UI in the postpartum period is lower after CS compared to vaginal delivery [Milsom 2009, Press 2007]. We know that there is more UI postpartum among women who had UI in pregnancy. Is it reasonable to assume that some women will benefit more than others from a CS to prevent UI postpartum?

There is only one article, nevertheless retrospective, presenting results stratified for continence status in pregnancy and then analysed on delivery parameters [Glazener 2006]. Glazener et al found (reanalysed) an OR 3.6 and 2.6 for UI after vaginal delivery among women who were continent and incontinent in pregnancy, respectively. It is unclear if this risk difference was significant. The absolute risk difference indicates that women with UI in pregnancy maybe should be advised to undertake CS to reduce risk of UI postpartum.

Generally, current evidence does not support the routine use of elective CS to prevent UI among any group of women [Lal 2003, Nygaard 2006]. New studies are however needed to clarify whether women with UI in pregnancy represent a group at higher risk of UI postpartum after vaginal delivery, and thereby should be recommended CS. To investigate how women with UI in pregnancy are affected by mode of delivery, we need results that are stratified for continence status in pregnancy and then analysed on delivery parameters.

1.8 Weight and weight gain as risk factors for UI

High weight and high BMI are established risk factors for UI at all ages both among men and women. The last 5 years several reviews regarding BMI and

UI have been published [Bart 2008, Greer 2008, Hunskaar 2008, Khong 2008, Subak 2009].

There are still many questions to be answer regarding weight as a risk factor. For instance; is BMI a better estimate than actual weight (kg), waist circumference or waist-hip ratio? Does the location of weight play a role? Is it only weight due to adiposity that leads to UI, or will muscles, oedema and pregnancy related weight also lead to UI? For how long must the weight have persisted to lead to UI? Is there a threshold weight? What are the mechanisms? Is weight an extraneous confounder for other risk factors? Chapter 1.8 will deal with problems and reflections on UI and weight that go beyond weight gain in pregnancy.

I will like to use an example to illustrate some of my points; Imagine a continent woman puts on a 20 kg backpack. How will this influence her risk of UI?

1.8.1 What do we know?

BMI is an established risk factor for UI. Both cross sectional studies [Hannestad 2003, Hunskaar 2004, Melville 2005] and longitudinal studies [McGrother 2006, Mishra 2008, Phelan 2009, Townsend 2007] have found an association between high weight and UI. Generally, overweight leads in general to an OR for UI of 1.5 – 3.0 compared to normal weight women, while obesity leads to an OR of 3.0 – 5.0.

Several cross sectional studies have found a dose response relationship between BMI and UI [Danforth 2006, Han 2006, Hannestad 2003, Larrieu 2004, Melville 2005]. The response relationship indicates that here might be a linear association between BMI and UI. RCTs on weight loss among obese women have found decreasing prevalence of UI after increasing weight loss [Brown 2006].

The severity of UI, estimated by Sandvik's severity index [Sandvik 2006] and other severity indexes based on frequency and volume escalates with increasing BMI [Danforth 2006, Hannestad 2003, Kuh 1999, Melville 2005, Sampselle 2002]. Townsend et al reported that the OR for severe UI increase with 3% for every kg weight gain [Townsend 2007].

1.8.2 What is unclear?

Type of study

Our woman puts on a 20 kg backpack. We ask her; "Are you incontinent?" Her answer will only be associated with the backpack if she reports incident UI. To say anything about the association between UI and weight, weight gain, threshold weight, induction time and so on, our outcome should be incidence of UI. The majority of epidemiological studies analysing BMI and UI are cross sectional and thereby report only prevalence of UI [Buchsbaum 2002, Chiarelli 1999a, Corcos 2004, Fultz 1999, Hannestad 2003, Hunskaar 2004, Kuh 1999, Melville 2005, Roe 1999, Rohr 2005, Simeonova 1990]. Several cohort studies have studied BMI and UI, but few reported data on incident UI according to BMI [Byles 2009, Mishra 2008, Townsend 2007]. One retrospective study has reported incidence of UI according to BMI [Santaniello 2007]. As it is very difficult to perform an RCT on weight gain, results from cohort studies are probably as far as we get.

What is "weight"?

Weight or weight gain?

If our woman at time point A does not wear a backpack, but at time point B wears a backpack, she will have experienced a weight gain during the A-B period. Her risk of UI at time point B can be associated with her weight at time point B or her weight gain during A-B. Weight and weight gain are two sides of the same story. Weight can be registered as a single static data point as in a

cross sectional study, while weight change is a dynamic variable relying on several observations; as in a cohort study.

Few studies have investigated the association between weight gain and UI [Mishra 2008, Townsend 2007]. The Nurses Health Cohort Study found that 1 kg/m^2 weight gain increased the risk of frequent UI with 7% [Townsend 2007]. The results indicate that here is a linear association, not only with absolute weight and UI, but also between weight gain and UI.

BMI vs. kg

BMI is estimated by weight (kg)/height (m)^2. The statistician Keys' introduced BMI in 1972 [Keys 1972]. BMI was explicitly cited by Keys as being appropriate for population studies, and inappropriate for individual diagnosis. If our woman puts on a 20 kg backpack, her increased BMI will not reflect the added weight and increased risk of UI, as her height^2 will partly camouflage the added weight. Most epidemiological studies use BMI when considering the association between weight and UI. Still, some studies find an explicit association between high weight measured in kg, not BMI [Townsend 2007]. If weight leads to UI through a mechanical process in the pelvis [Bump 1992], the absolute weight (kg), and not the relative weight (BMI) is interesting.

What does BMI represent?

BMI is a measurement of relative weight, a surrogate measurement with no indication of body composition. Does it matter if the weight gain is due to a backpack, pregnancy, muscles, oedema or adiposity? Many studies confirm the relationship between high BMI due to adiposity and UI. Weight gain in pregnancy is mainly due to a growing foetus, placenta and uterus, enlarged breasts and oedema. Weight gain appears to have a different impact on UI in pregnancy (Table 7) than in other time periods of life. There are no studies investigating whether a BMI due to muscles also might lead to UI. When Arnold Schwarzenegger won Mr Olympia he had a BMI of 31. Athletes have a

higher mean diameter of the perineal muscle [Kruger 2007]. Even thought athletes also leak, higher mean perineal diameter might be protective of UI [Stav 2007]. They sometimes gain the pelvic characteristics found among women with stress UI, but without having UI [Kruger 2007]. It is likely that high weight leads to UI mainly through adiposity, but studies are needed to investigate the association between a study population with high muscle mass, a study population with oedema or a pregnant study population and UI.

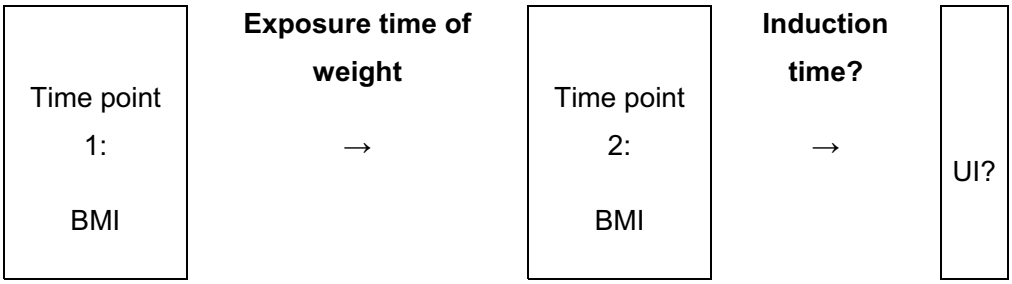
Location of weight gain

Will the risk of UI be the same if our woman puts the backpack on her back, abdomen or around her waist? Several studies have reported that waist circumference was predictive for stress UI [Hannestad 2005, Townsend 2008], even after adjusting for BMI [Han 2006, Hannestad 2005]. Another small cohort study found that reduction in waist circumference explained the effect of reduced BMI on UI [Subak 2005]. Waist – hip ratio is also found to be an independent risk factor for stress UI [Brown 1999, Hannestad 2005]. Studies on pregnant women have found that weight gain during pregnancy is not associated with UI (Table 7). This might indicate that pressure directly on the pelvis predicts UI while weight with a vector that does not put direct pressure on pelvis (a backpack, a large pregnant abdomen, leg oedema, etc) might not predict UI.

Weight period

If our woman puts on an open backpack that gradually fills up with 20 kg rainwater, will she experience the same risk of UI as if she puts on a 20 kg backpack at once? Few studies have investigated the association between UI and the exposure time of the measured weight (Figure 1).

Figure 1. Exposure time and induction time of weight in the association with UI



Exposure time and speed of weight gain

Mishra et al found that women who had been overweight from age 26 – 54 were more likely to be incontinent than women who became overweight after the age of 54 [Mishra 2008]. Several articles present results indicating that a large weight gain in pregnancy does not lead to UI [Diez-Itza 2009, Eason 2004]. Is it possible that weight gain must have persisted for a certain time (more than 9 months?) to lead to UI?

Another aspect is how fast the weight increases. Townsend et al reported an OR 1.9 for UI among women who gained > 30 kg over 28 years, an OR 2.5 among women who gained > 30 kg over 12 years and an OR 3.5 among women who gained > 20 kg during 4 years [Townsend 2007]. It appears that weight gain over a short time period increased the risk of UI more than weight gain over a long time period. If so, why does not weight gain in pregnancy lead to UI?

Induction time

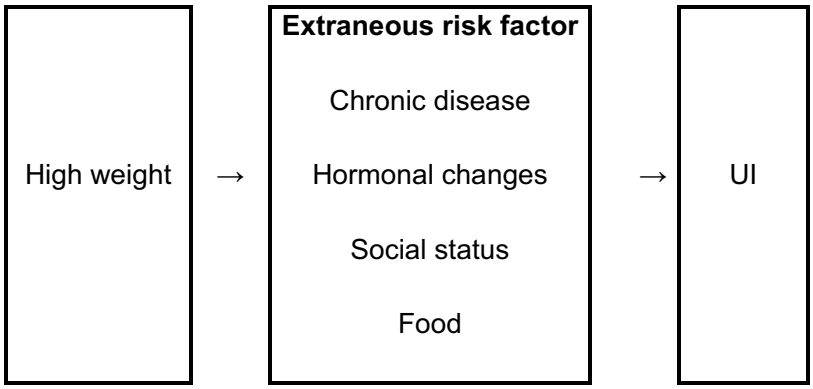
If our woman puts on the 20 kg backpack this morning, she will probably not be incontinent this evening. It will take some time to develop UI; there will be an induction time from the exposure “weight gain” to manifestation of the outcome “UI” (Figure 1).

SVD is an example of a risk factor for UI with a short induction time. Childhood enuresis has a long induction time as it increases risk of incident UI among adult women [Brown 2010]. In cross sectional studies on BMI and UI there is no information about induction time. Cohort studies have a time period between BMI and UI. We do, however, not know if this represents the whole induction time.

Will high weight during the induction time induce physiological changes in the pelvis that take time to bring out into clinical symptoms? One author claims that overweight stress the pelvic floor through a statistically significant change in measures of intra-abdominal pressure [Noblett 1997]. Increasing intra-abdominal pressure is linear with weight, and pressure is reduced by weight loss. This indicates no induction period between weight gain and UI. We are, however, not sure that intra-abdominal pressure is the only link between overweight and UI. Other processes might be slow acting, like chronic strain, stretching and weakening of the muscles, nerves, ligaments and other structures of the pelvic floor etc but few studies have been able to demonstrate this [Milsom 2009]. The biological cause for weight to lead to UI might indicate the induction time.

Weight as an extraneous/confounding risk factor

Figure 2. Extraneous risk factors for the association between weight and UI.



Weight or chronic disease

Will our woman develop arthritis and therefore later develop UI? High BMI is related to several chronic diseases; hypertension, diabetes, coronary disease, stroke, asthma, arthritis, depression, cancer and neuropathy. Several of these diseases are also associated with UI; hypertension [Song 2005], coronary heart disease [Shakir 2007], asthma [Phelan 2009], arthritis [Phelan 2009] and depression [Phelan 2009, Sung 2009]. Some diseases, like diabetes and stroke, are still risk factors for UI even after adjusting for BMI [Byles 2009, Ebbesen 2009]. People with UI will in general report lower health status than people without UI [Roe 2000]. Can disease itself cause UI, and not the weight? (Figure 2) Asthma might lead to coughing, diabetes might lead to neuropathy, stroke might lead to autonomic damage that influence continence, hypertension and coronary heart disease might indicate cardiovascular disease in pelvic region. Studies that have data on these diseases ought to take these factors into consideration when investigating the relationship between weight and UI.

Weight or weight related hormonal changes

Will our woman with the backpack gradually develop UI due to hormonal changes in the body? Adiposity leads to different levels of several hormones; increased levels of cortisone, insulin, leptin, relaxin and reduced levels of FSH, LH, inhibin B, SHBG and testosterone. Most studies confirm that estradiol levels increase with high BMI [Karim 2009], but results are not consistent [De Pergola 2006]. These hormones influence the body in several ways.

Some studies have found estradiol levels to be a risk factor for UI, even after adjusting for BMI [Gopal 2008, Teleman 2009]. Also, studies have found no association between estradiol and UI [Litman 2007, van Geelen 1982], while others have found a protective effect [Thielemann 2009]. Studies have found no association between increased levels of cortisone, testosterone [Teleman 2009] or SHBG [Litman 2007] and UI. Data on UI and relaxin are unclear

[Kristiansson 2001]. Weight influences hormone levels. We do not know the mechanisms for these hormonal changes to lead to UI. We cannot rule out that UI is caused by endocrine changes rather than by adiposity itself (Figure 2). Future studies with bio bank data are needed to investigate these associations further.

Weight or social status

Will a woman who carries all her belongings in a backpack have higher risk of UI due to factors associated with low social status? Low social status has been found to be associated with UI [Karakiewicz 2008]. The other way around, UI has also socioeconomic implications [Temml 2000]. Low social status is associated with several characteristics: smoking, higher alcohol consumption, low educational level, low income and unemployment, race, marital status, more children, less physical activity and poor self reported health. Overweight is also a larger problem among people in lower social classes. All the above characteristics of low social class are in studies found to be associated with UI, but there is no consistency in the literature. It is difficult to find biological explanations for several of these findings. Some studies find that the above characteristics are risk factors even after adjusting for BMI. Unfortunately, most studies investigating the association between BMI and UI do not take variables associated with social status into account. There is need for further studies on weight and potential confounders. We can not rule out that socioeconomic status have a role in UI, and that BMI and social status interact as risk factors (Figure 2).

Weight or food

Is it the weight of the backpack or what you put in the backpack that leads to UI? There is a close relationship between unhealthy saturated fatty food and adiposity. Intake of total fat and saturated fatty acids is linked to increased risk of stress UI after adjusting for BMI [Dallosso 2004]. This indicates that there

might be an association between certain components in the diet and the onset of UI (Figure 2). The mechanisms behind this finding are, however, unclear.

BMI and pregnancy

Many studies have found pregnancy per se to be a risk factor for increased prevalence of UI both in pregnancy [Hojberg 1999] and several years later [MacLennan 2000, Rortveit 2003a]. A general theory is that the increased UI in pregnancy is due to weight gain [Milsom 2009]. However, previous studies indicate that the increased incidence of UI in pregnancy is not due to weight gain [Chiarelli 1997, Diez-Itza 2009, Eason 2004, Glazener 2006, Kristiansson 2001, Pregazzi 2002, Sottner 2006, van Brummen 2007] (Table 7).

Weight gain in pregnancy is normal

Will our woman have lower risk of weight induced UI if she puts on the backpack while she is pregnant? No studies have been designed to investigate the association between weight gain and UI in association with pregnancy. However, studies dealing with this association have not found a clear association, neither with UI in pregnancy nor postpartum (Table 7).

Pregnancy is a normal physiological state for women, necessary from an evolutionary point of view. Overweight, however, is not. Pregnancy affects the female body in several ways; both mechanically, psychologically and last but not least hormonally. A hypothesis is that weight gain in pregnancy is not associated with UI due to other pregnancy related changes. Some studies have found oestrogen to have a protective effect on UI [Thielemann 2009]. Oestrogen levels increases markedly during 3rd trimester. Some studies have found no association, and even negative associations, between oestrogen levels and UI [Hendrix 2005]. These levels of oestrogen in the latter studies were, however, much lower than what is normal in pregnancy.

Table 7. The association between UI and weight gain in pregnancy

	Origin	Study	N	Data collection	Time	Ass. with weight gain and UI in pregnancy	Ass. with weight gain and UI postpartum
[D'Alfonso 2006]	Italy	Cross-s	120	Interview	30 days PP	+	+
[Chiarelli 1997]	Australia	Cross-s	304	Interview	Postnatal	-	
[Diez-Itza 2009]	Spain	Cohort	458	Interview, ex.	At delivery	-	
[Eason 2004]	Canada	Cohort	949	Questionnaire	Week 30, 3 mth PP	-	-
[Glazener 2006]	UK. New Zealand	Cross-s	3,405	Questionnaire	3 mth PP		-
[Kristiansson 2001]	Denmark	Cohort	200	Examination	Week 36	-	
[Pregazzi 2002]	Italy		537	Inerv., ex.	3 mth		-
[Sottner 2006]	Czech republic	Cross-s	339	Questionnaire	At delivery.	-	
[Troiano 2000]	Italy	Cross-s	537	Quest.., ex.	3 weeks PP		+
[van Brummen 2007]	Netharland	cohort	334	Questionnaire	12 mth PP		-

cross-s = cross sectional study, Quest. = Questionnaire, Interv- = interview, Ex. = examination, PP = postpartum, Ass. = association

We do not know the answer to why there is no association between weight gain and UI in pregnancy and postpartum. Maybe there are two weight gain stories: one for pregnant women and one for everyone else? Also, we do not know exactly why UI peaks in pregnancy. There is need for studies designed to investigate this association.

What type of UI is associated with high weight?

If our woman puts on a 20 kg backpack; is she more prone to stress UI than urge UI? Stress UI is the type UI most closely associated with high weight [Alling Moller 2000, Hannestad 2003, Mommsen 1994]. It does not appear to be such a close association between high weight and urge UI. When looking at the dose response association, results are, however, not consistent. Cross sectional studies have investigated the association between weight and UI. In several studies, all involving > 1000 participants, the dose response association for type of UI for every 5 unit BMI varies; some studies find a stronger association between stress UI than urge UI [Hannestad 2003, Jackson 2004, Song 2005]. One study found an even risk for stress UI and urge UI [Brown 1999]. Finally, one study found a stronger association for urge UI than stress UI [Kuh 1999].

Some cohorts have investigated the association between weight and type of UI. Studies confirm that stress UI is more strongly associated with high weight than urge UI [Burgio 2007b, Dallosso 2003, Mishra 2008, Phelan 2009, Townsend 2008, Townsend 2007, Waetjen 2007]. However, also in cohort studies the results are not uniform. A large study on weight and UI found that BMI was associated with urge and mixed UI, but not stress UI [Townsend 2008]. Even thought the general impression is that high weight leads to mainly stress UI, results are not consistent.

1.8.3 Conclusion on weight and weight gain

Although few would doubt that weight plays a role in UI, it has been difficult to demonstrate exactly how it acts. Today's knowledge tells us that there are associations between weight and any UI and severity of UI, and the strength of the association increase with high weight.

There are still many unanswered questions for future studies on UI and weight: What does a high BMI represent: muscles, pregnancy, oedema or body fat? Is only adiposity linked to UI? Is BMI the best variable for the association with UI, or is location of weight measured by waist-hip-ratio, waist circumference, total body fat, or visceral fat better variables? There is need for prospective studies, preferably lifelong studies with several follow-ups, investigating the duration and induction time of weight and weight gain's association with incident UI. Overweight are associated with several conditions, social characteristics, distinguished food intake, and hormonal changes. Studies should try collect these (biological) data and take these variables into account when analysing on UI. Outcome of future studies on weight and UI should differentiate between the types of UI.

The hypothesis on BMI and UI is likely to be elaborated upon in future studies on weight and UI.

2. The present study

2.1 Aims of the study

The aims of the present study were to investigate incidence, prevalence and risk factors for UI in a cohort of pregnant women.

- *Sub study I.*

The aims of this study were to investigate incidence and prevalence of UI in pregnancy, in addition to investigate associated risk factors for UI in pregnancy. Results are presented in **Paper I**.

- *Sub study II.*

The aims of this study were first to investigate the incidence and prevalence of UI 6 months after delivery; second, to investigate the impact of continence status in week 30 of pregnancy on UI 6 months postpartum and third, to investigate how mode of delivery may interact with continence status in pregnancy to increase or reduce the risk of UI 6 months postpartum. Results are presented in **Paper II**.

- *Sub study III.*

The aim of this study was to investigate how the incidence of UI in pregnancy was affected by weight gain in pregnancy. We also investigated how incidence and prevalence of UI 6 months postpartum were affected by weight changes in pregnancy and postpartum. Results are presented in **Paper III**.

2.2 Material and methods

2.2.1 The Mother and Child Cohort Study

The present study is based upon data from The Mother and Child Cohort Study (MoBa). The superior goal for The MoBa study was to achieve better health for mothers and children in the future, primarily through prevention. The background for the MoBa study was the lack of understanding about the cause of disease in association with pregnancy. Among many things, the MoBa was carried out with the intention to aid the development of new medicines through new methods in genetic epidemiology, to reduce unwarranted anxiety among pregnant women, to examine quality of life and positive aspects of health, and to examine commonly held beliefs concerning the causes of disease [Magnus 2005].

The MoBa project was initiated by MBRN in Bergen and the Norwegian Institute of Public Health in Oslo. The MoBa study was anchored at The Norwegian Institute of Public Health, Division of Epidemiology, which also includes MBRN located in Bergen [Magnus 2005].

There are approximately 60,000 births in Norway annually. To test specific hypotheses about the cause of a number of diseases, the target sample size of MoBa was 100,000 pregnant women who were to be recruited nationally between 1999 and 2006. Due to lower response rates than expected (45 %), 100,000 women were before the summer of 2009.

An invitation for participation in the study was sent to women at their home address. The majority of pregnant women received this package 3 weeks before attending routine ultrasound examination in week 17 of pregnancy (Figure 3). A total of 39 of about 50 hospitals and maternity units in Norway with more than 100 births annually participated in the study. Names and

addresses of pregnant women were obtained from the maternity unit that had received a request for ultrasound examination.

Figure 3. Questionnaires in the Mother and child cohort study used in our study [Magnus 2005]

Responsible insititution :			
Week/mth	**Hospital**	**MBRN**	**Inst.of public health**
10 – 14 (Before ultrasound)	Received name and address of pregnant women from referring GP. A copy of list sent to MBRN each week	Sends invitation by post to women with Questionnaires 1 and 2. Receives consent form and questionnaires from participating mothers and fathers.	
17 (Ultrasound examination)	Women are asked if they will participate. Blood sample taken.	Receive copy of standard ultrasound form	Receive blood sample from mothers and fathers.
18 – 33 (later in pregnancy)		Reminder fro missing consent form and Questionnaireionnaires. Send out Questionnaire 3 in week 30 Reminder sent 3 weeks later	
Birth	Blood sample from mother and umbilical cord after birth		Receive blood sample from mother and child
6 months post partum		Send out Questionnaire 4	

Each week the ultrasound clinics sent a list of all women who had appointments to the MBRN. The invitation, which was sent out in collaboration with each participating hospital, described the purpose of the study, protection of privacy and practical details. It was emphasized that participation was voluntary. The women were also notified that they could withdraw at any time. Information brochures about the project and the MBRN were enclosed, together with Questionnaire 1 and 2 (Figure 3). Also enclosed was a consent form, which required a signature, and a return-paid envelope. If the women accepted to participate in the MoBa, six future Questionnaires to mother and/or father and one blood sample from mother, father and child was

collected. Questionnaire 3 was sent out in week 30 of pregnancy, Questionnaire 4 was sent out 6 months post partum (www.fhi.no). **Papers I – III** are based upon Questionnaire 1, 3 and 4. Further questionnaires regarding mother and child's health were sent out 18 and 36 months post partum. Questionnaires on child's health only were also sent out when the child was 5 and 7 years old.

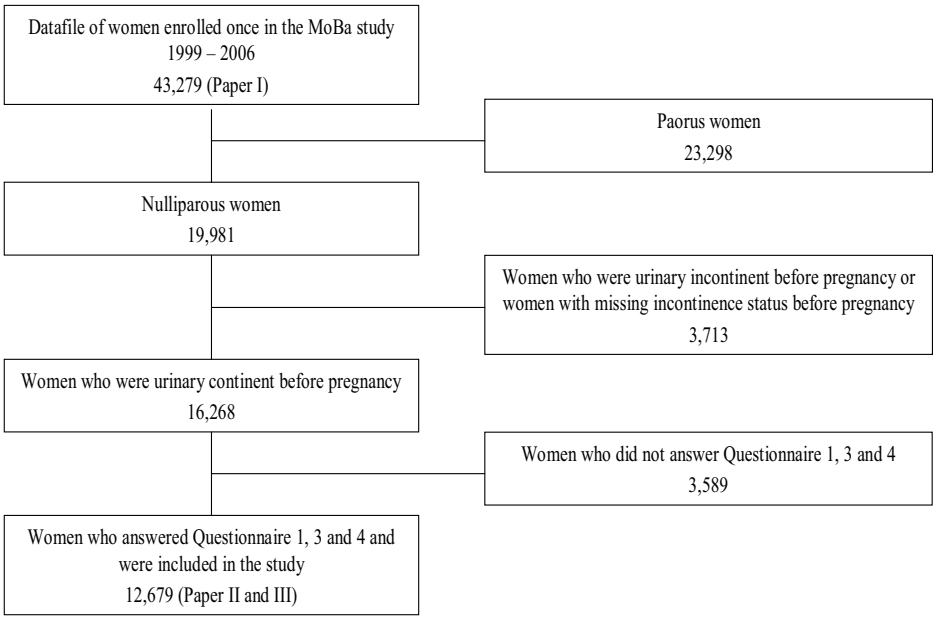
Images of the returned questionnaires were scanned. A database was constructed for each of the questionnaires. A working group carried out quality controls during and after the scanning process and before final storage, and made sure manual entering of specific variables was carried out if required. Questionnaires having passed through the quality control were stored in the databases. Files intended for use by researchers for analysis, were given out in SPSS format [Magnus 2005].

The MoBa information from questionnaires and blood samples were linked to medical registries. No intervention was undertaken in the MoBa study. MoBa was open for researchers from both basic and applied research. The focus for research on MoBa data could be child, birth or mother. We focused on the mothers.

In **Paper I**, available dataset at the time (April 2006) that included Questionnaire 1 and Questionnaire 3 were used. All women who had contributed with more than one pregnancy were excluded (n=2,983). **Paper I** was based on a sub study dataset of 43,279 women.

Paper II and **Paper III** use the same dataset. This time the study population was restricted to women who had answered Questionnaire 4 in addition to Questionnaire 1 and 3. In addition, we excluded all parous women and all women who were incontinent before pregnancy. Women who did not report continence status before pregnancy were also excluded. **Paper II** and **Paper III** are based on a sub study dataset containing 12,679 women (Figure 4).

*Figure 4. Participants in **Paper I, Paper II** and **Paper III***



In October 1996, the project was granted a concession by the Norwegian Data Inspectorate. This was renewed in September 2003. The project is partly financed by the Ministry of Health and has been approved by the Norwegian Parliament.

2.2.2 The Medical Birth Registry of Norway

The MoBa data was linked to MBRN, which holds information on all births in Norway from 1967. All maternity units in Norway report name, personal identification number and several data regarding mother's health before and in pregnancy, data regarding delivery and possible complications during labour, and data on the child on a notification form which is sent to the MBRN (Appendix 4). The dataset from MBRN was included in the data we received from MoBa. If the MBRN did not have information on previous births, the women were defined as nulliparous and included in this study.

2.2.3 Questionnaires

The women received a 14 – 18 pages questionnaire in week 15, week 22 (focus on diet) and week 30 of pregnancy, 6 months postpartum, 18 months, 3 years, 5 years (sent out for the first time in 2010) and 7 years after birth. The latter questionnaires focus mainly on the child. In addition, the father received a questionnaire in week 15. Mother gave blood and urine sample at ultrasound examination; father gave a blood sample at the same time. At birth a blood sample was taken from mother and from the umbilical cord of the baby to be stored in the bio bank.

In **Paper I** we used questionnaire data from questionnaires received in week 15 (Questionnaire 1) and 30 (Questionnaire 3). In **Paper II** and **Paper III** we used questionnaire data from Questionnaire 1, Questionnaire 3, in addition to data from Questionnaire 4 sent out 6 months postpartum (Figure 4). (See appendix 5 – 7 for questions with UI variables, see "http://www.fhi.no/eway/default.aspx?pid=233&trg=MainArea_5661&MainArea_5661=5631:0:15,2301:1:0:0:::0:0&MainLeft_5631=5544:42547::1:5641:1:::0:0 " for full questionnaires (or use the following navigation: www.fhi.no, choose "mor og barn-undersøkelsen", choose "Spørreskjemaer")).

In Questionnaire 1 (Appendix 5), only question 39 was dedicated UI:

“Did you have UI before pregnancy?” yes/no. Questions about UI before pregnancy in Questionnaire 3 also contained data on type, frequency and amount. Therefore data on UI before pregnancy was taken from Questionnaire 3.

In Questionnaire 1, we used question 37 regarding weight: “What was your weight when you became pregnant, and what is your weight now?”

In Questionnaire 3 (Appendix 6), question 28 was dedicated UI:

1) “Before this pregnancy, did you experience incontinence when coughing, sneezing or laughing?” Answering alternatives were; “yes”/”no”. Frequency alternatives: “1-4 times a month”, “1-6 times a week”, “Once a day”, “More than once a day”. Amount alternatives: “Drops”, “Large amounts”.

2) “Before this pregnancy, did you experience incontinence during physical activity (running/jumping)?” Answering alternatives were; “yes”/”no”. Frequency alternatives: “1-4 times a month”, “1-6 times a week”, “Once a day”, “More than once a day”. Amount alternatives: “Drops”, “Large amounts”.

3) “Before this pregnancy, did you experience incontinence with a strong need to urinate?” Answering alternatives were; “yes”/”no”. Frequency alternatives: “1-4 times a month”, “1-6 times a week”, “Once a day”, “More than once a day”. Amount alternatives: “Drops”, “Large amounts”.

Question 1-3 was repeated, starting with “In this pregnancy, have you experienced…..”

In Questionnaire 3, we used question 25 regarding weight: “How much did you wheigh at your last antenatal check-up?”

In Questionnaire 4 (Appendix 7), question number 54 regarding UI was phrased the same way as questions regarding UI in Questionnaire 3.

In Questionnaire 4, we used question number 69 regarding weight: “How much did you weigh at the end of your pregnancy, and how much do you weigh now?

The UI questionnaires currently used in MoBa were changed after we received our present data file. The current questionnaires presented at the web are not all expressed and typed in the same way as the attached files in the Appendix, which are the questionnaires used in the current study.

The definition of any UI in **Paper I** – **III** was based on the above questions. All women who answered conformingly on the UI questions, and/or reported frequency of UI and/or reported amount of UI were defined as urinary incontinent in **Paper I** – **Paper III**.

2.2.3 Analyses

The MoBa dataset was primarily analysed in SPSS. STATA was used for log binomial regression analyses.

A variable was included in multivariable regression analyses as a confounder if the variable affected both the prevalence of the exposure and the outcome, and made a difference to the risk of UI associated with the exposure. We explored age, BMI, sex of baby, head circumference, baby’s weight, Apgar score (1 and 5 minutes), fetal presentation at delivery (normal occipital, breech, transverse, abnormal fetal head presentation and other), birth time (minutes), prolonged labour, perineal tear grade 3–4 and induction (amniotomy, oxytocin and prostaglandins), training, and breastfeeding.

Effect modification of continence status on the effect of SVD compared with elective CS on UI was tested by use of interaction terms in multivariable logistic regression analyses in **Paper II**.

Paper I presents risk parameters as OR. In **Paper II** all ORs and corresponding CI were converted to RRs and corresponding CI by use of the

formula RR = OR/((1 – P) + (OR x P)) [Zhang 1998]. In this formula, P is the prevalence of UI in the unexposed group. In **Paper III** log binomial regression analyses were used to present risk parameters as RR.

3 Main results

3.1 Paper I

Wesnes SL, Rortveit G, Bo K, Hunskaar S. (2007), Urinary incontinence in pregnancy. Obstet Gynecol, 109: 922 – 928.

Aim: Investigate incidence and prevalence of UI in pregnancy, and investigate risk factors associated with UI in pregnancy.

We used questionnaire dataset available from MoBa at the time, containing 43,279 women (response rate 45%) by week 30 of pregnancy. We reported data on any UI, in addition to type, frequency, and amount of UI. Potential risk factors were investigated by logistic regression analyses.

The mean age at the time of filling in Questionnaire 3 was 29.5 (range 14–47) years. The mean number of deliveries before the present pregnancy was 0.8 (range 0–10). The prevalence of UI increased from 26 % before pregnancy to 58 % in week 30. The corresponding figures for nulliparous women were 15% and 48%, and for parous women 35% and 67%. The cumulative incidence was 46%. In week 30, 31 % of nulliparous and 42 % of parous women experienced stress UI. The majority of pregnant women experienced only minor frequency and amount of leakage. Parity was a strong and significant risk factor for UI in adjusted analyses both before pregnancy (OR 2.5, 95% CI 2.4 –2.7 for nulliparous and OR 3.3, 95% CI 3.1–3.5 for multiparous women) and in pregnancy (ORs 2.0, 95% CI 1.9 –2.1 and 2.1, 95% CI 2.0 –2.2, respectively). Age > 26 years and BMI > 20 kg/m^2 were weaker, but still statistically significant, risk factors.

We concluded that the prevalence of UI increases substantially in pregnancy. UI both before and in pregnancy was associated with parity, age, and BMI.

3.2 Paper II

Wesnes SL, Hunskaar S, Bo K, Rortveit G. (2009), The effect of urinary incontinence status during pregnancy and delivery mode on incontinence postpartum. A cohort study. BJOG, 116: 700 – 707.

Aim: First to investigate the incidence and prevalence of UI 6 months after delivery; second, to investigate the impact of continence status in week 30 of pregnancy on UI 6 months postpartum and third, to study how mode of delivery may interact with continence status in pregnancy to increase or reduce the risk of UI 6 months postpartum.

We used questionnaire data from nulliparous women who were continent before pregnancy who had answered Questionnaire 1 (week 15), 3 (week 30) and 4 (6 months postpartum). The study population thereby consisted of 12,679 of the women from **Paper I**. Data was linked to MBRN. Mode of delivery was categorised as elective CS, acute CS intended as elective CS, acute CS intended as SVD, unspecified CS, SVD, forceps delivery and vacuum delivery. Confounding was thoroughly evaluated and adjusted for by multivariable logistic regression analyses and crosstabs analyses. Effect modification of continence status on the effect of SVD compared with elective CS was tested by Breslow – Day. We treated independent variables as categorical. Due to UI being a very common condition, all OR and CI were converted to RR.

Mean age was 28 years (range 15–45 years), and mean BMI was 24.1 kg/m2 (range 14–54 kg/m2). A total of 14 % of the study population had delivered by CS. UI was reported by 31% of the women 6 months after delivery. Incidence of UI 6 months postpartum among women who were continent before and in pregnancy was 21 %. Compared with women who were continent in pregnancy, UI was more prevalent 6 months after delivery among women who experienced UI in pregnancy (adjusted RR 2.3, 95% CI 2.2–2.4).

The strongest associated factors for incident UI in adjusted analysis were forceps delivery (RR 4.0, 95% CI 2.6–5.8), SVD (RR 3.2, 95% CI 2.1–4.7), vacuum delivery (RR 3.2, 95% CI 2.1–4.7), all compared with elective CS. The different types of CS did not represent significant risk factors for UI 6 months postpartum. Compared with elective CS, the adjusted RR for UI 6 months postpartum after SVD was 3.2 (95% CI 2.5–3.9), after vacuum 3.3 (95% CI 2.6–4.0), and after forceps 3.5 (95% CI 2.6–4.4).

Adjusted RR for incontinence after SVD compared with elective CS was 3.2 (95% CI 2.2–4.7) among women who were continent and 2.9 (95% CI 2.3–3.4) among women who were incontinent in pregnancy. By Breslow-Day we did not find statistically significant difference in the risk estimates.

We concluded that there was a considerably raised risk for UI postpartum among those who developed UI in pregnancy compared with those who were continent. The association between incontinence postpartum and mode of delivery was not substantially influenced by incontinence status in pregnancy. Prediction of a group with high risk of incontinence according to mode of delivery cannot be based on continence status in pregnancy.

3.3 Paper III

Wesnes SL, Hunskaar S, Bo K, Rortveit G. (2010) Urinary incontinence and weight gain in pregnancy: a cohort study. Am J Epidemiol, 172: 1034 – 1044

Aim: Investigate how the incidence of UI in pregnancy was affected by weight gain during weeks 0–15 and 15–30 of pregnancy. We also investigated how incidence and prevalence of UI 6 months postpartum was affected by weight gain during weeks 0–15, 15–30, 30–delivery, and 0–delivery; by weight gain from week 0 of pregnancy to 6 months postpartum; and by weight loss from delivery to 6 months postpartum.

We used the same MoBa data material in **Paper III** as in **Paper II**; 12,679 nulliparous women who were continent before pregnancy who had answered Questionnaires 1, 3 and 4. We categorised weight gain and weight loss into 1 – 50 percentile, 51 – 90 percentile and > 90 percentile to investigate the effect of weight change beyond the median and also isolate the effects of extreme weight change. Data were stratified for underweight, normal weight and overweight women. We treated independent variables as categorical, whereas weight gain and weight loss were also treated as continuous variables in logistic regression analyses. We evaluated the assumption of a linear trend between weight change and UI through model comparisons using chi squared tests. The assumption of linearity could not be rejected (P = 0.65 for weight gain and P = 0.06 for weight loss). Adjustment for confounding was done by multivariable logistic regression for the different time periods. We used STATA for log binomial regression analyses in order to present risk parameters as relative risks.

Mean weight change during week 0 – 15 was 3.3 kg, week 15 – 30 was 7.0 kg, week 30 – delivery 6.3 kg, week 0 – delivery 15.8 kg, week 0 – 6 months postpartum 1.2 kg and delivery – 6 months postpartum -14.5 kg. Weight gain > 50th percentile during weeks 0–15 of pregnancy was weakly associated with higher incidence of UI at week 30 compared with weight gain ≤ 50th percentile, but not associated with UI 6 months postpartum. The effect of weight gain on UI led to the highest risks among underweight women.

Weight gain > 50th percentile in pregnancy was not associated with increased prevalence of UI 6 months postpartum. Weight gain > 50th percentile and > 90th percentile from start of pregnancy to 6 months postpartum was more strongly associated with having UI than was high weight gain in any single sub period in analyses of all women (RR 1.2, 95% CI 1.1 – 1.2 and RR 1.3, 95 % CI 1.2 – 1.4, respectively). The same trend was found in stratified analyses. For each kg weigh gain from week 0 – 6 months postpartum, the RR of UI 6 months postpartum increased by 2.3 % (RR 1.02, 95 % CI 1.02 – 1.03).

Weight loss > 50th percentile and > 90 percentile postpartum among women who were incontinent in pregnancy lead to a statistically significant risk reduction on UI (RR 0.9, 95 % CI 0.8 – 0.9 and RR 0.7, 95 % CI 0.6 – 0.8, respectively). The findings were reproduced among normal weight and overweight women. For each kilogram of weight loss from delivery to 6 months postpartum among women who had UI in pregnancy, the RR for UI decreased 2.1% (RR 0.98, 95% CI 0.97, 0.99). Among women who were continent in pregnancy, the risk of incident UI 6 month postpartum also decreased with increasing weight loss (> 50th percentile RR 0.8, 95 % CI 0.7 – 0.9 and > 90th percentile RR 0.7, 95 % CI 0.5 – 0.8). Corresponding associations were found in stratified analyses among normal weight and overweight women.

We concluded that weight gain in pregnancy does not seem to be a clinically important risk factor for UI. However, weight loss postpartum may be important for avoiding incontinence and regaining continence 6 months postpartum.

4 Discussion

4.1 Methodological considerations

As all papers originate from the same data material, I will discuss methodological considerations in a common chapter.

4.1.1 Methodological strengths

The MoBa study and the Danish National Birth Cohort [Jacobsen 2010] are considered the most comprehensive international pregnancy cohorts. The Danish National Birth Cohort and the MoBa started recruiting women in 1996 and 1999 respectively, both aiming at enrolling 100,000 pregnant women. By 2011 only MoBa has recruited 100,000 women.

As the MoBa data file was linked to validated MBRN data, the database has unique possibilities to explore UI in association with pregnancy. The MoBa study invited all pregnant women in Norway to participate, underscoring that the target population of MoBa was unselected and population-based. Cohorts on UI in pregnancy and postpartum rarely exceed > 1,000 participating women [Brown 2010, Solans-Domenech 2010]. In 2006 Glazener wrote in their article; “With responses from around 3405 women who were primiparae, this is the largest study to date examining the relationship between onset of incontinence, pregnancy and other potential confounding factors.” [Glazener 2006] By 2011 the study population in **Paper I** was the largest study population in cohorts on UI in pregnancy. **Paper II** and **III** was the largest cohorts based on nulliparous women.

External validity

External validity refers to whether or not the results can be generalised to a population beyond those who participated in the survey. High external validity is regarded as the main advantage of a population-based cohort studies as MoBa. The best way to be able to say something about everybody is to include

everybody. This is what MoBa intended to do. If MoBa had succeeded in including everybody, the external validity would be high.

The MoBa study was intended as a population based study including all pregnant women from 50 out of 52 maternity units with > 100 birth/year in Norway. Nearly all pregnant women in Norway are referred to routine UL in week 18. All women who belong to the respective maternity units were invited to the study when referred to UL examination.

Participation rates for epidemiologic studies have been declining internationally during the past 30 years with even steeper declines in recent years [Galea 2007]. It has been increasingly difficult to achieve high participation rates in cohort studies like MoBa. There may be many reasons for the low participating rate [Galea 2007]; for instance resistance to commitment in a comprehensive study with questionnaires of 16 pages. The response rate in MoBa in 2005 was 43 % [Magnus 2006]. By 2007, the recruitment rate was 40 % (89,594/222,484). The recruitment rate dropped when invited the second time. Response rate was therefore somewhat higher for nulliparous women (45 %). The Danish National Birth Cohort, which has a similar design as the MoBa study, has an overall response rate of 31 % [Jacobsen 2010].

Selection bias due to low recruitment has to be addressed. MBRN has data on women who did not participate in MoBa. One study shows only minor differences in parity, age, preeclampsia, gestational age, preterm birth, birth weight and low birth weight between participating and non – participating women [Magnus 2006]. A recent study, however, conclude that there are statistically significantly relative differences in prevalence estimates between cohort participants and the total population for several variables; young age (< 25), chronic hypertension and smokers, to mention some factors [Nilsen 2009]. Still, there is no reason to believe that there was a selection on the basis of UI status since the MoBa was a survey covering many topics, and UI questions only being a minor issue.

Still, women in lower socio-economic classes were underrepresented in the MoBa [Magnus 2006]. This is in line with results from the Danish National Birth Cohort [Jacobsen 2010] .The literature is inconsistent regarding the association between income, level of education and UI [Burgio 2007a, Torkestani 2009]. We cannot rule out that there was a selection bias arising from socioeconomic factors affecting our prevalence data. If there is a higher prevalence of UI among women with low income and low level of education, the incidence and prevalence estimates in our study were underestimated. Risk factors such as BMI, age and parity are likely to be distributed differently among women with low income as compared to women with higher income. However, a recent study from MoBa found no statistically relative differences in association measures between participants and the total population, and the authors concluded that effect estimates for risk factors were not affected by selection bias in the MoBa [Nilsen 2009]. We therefore believe that the presented risk estimates for UI are not affected by selection bias.

Cohort follow-up rates affect external validity. A strong point in the MoBa study was that the participating women remained in the study. The follow up rate when included in the study was high; of women filling in Questionnaire 1, 93 %, 92 % and 87 % filled in Questionnaire 2, Questionnaire 3 and Questionnaire 4, respectively [Magnus 2006].

Exclusion and inclusion of participants in our study should lead us to be conscious about generalisation. We have included only mothers with one foetus. In **Paper II** and **Paper III** we only included women who were nulliparous and continent before pregnancy. It is therefore difficult to generalise the results to all obstetric wards or general practices. Isolated, we can for instance not say that weight loss postpartum is efficient for avoiding UI for any other population but primiparous women who were continent before pregnancy. In particular, **Paper III** is a hypothesis - generating paper trying to identify new associations and to test so called “established truths” (high BMI

leads to UI). It will be up to future studies to identify whether or not these findings are valid for other populations.

Different distribution of demographic variables such as age, BMI, ethnicity, parity, mode of delivery etc in different populations outside Norway will decrease the external validity of our results in these settings. Our results are adjuseted and stratified for age, BMI and mode of delivery were appropriate. Our results will therefore have hight external validity in regions with different distribution of these variables. Still, our results will have lower external validity in regions were demographic variables (apart from age, BMI, mode of delivery) are distributed differently. As described under “Discussion of results” there are, however, striking similarities with effect estimates from both Australian and American UI studies [Brown 2010, Burgio 1996].

Based on studies on MoBa data [Magnus 2006, Nilsen 2009] we conclude that the prevalence estimates, but not the effect estimates, might be affected by a socioeconomic selection bias. Our findings in **Paper I** appear to have high external validity in Scandinavia, America and Australia. **Paper II** and **Paper III** are hypotheses – testing and based on a study population consisting of nulliparous women who were continent before pregnancy. Cautions should be taken in generalising these results to other groups of pregnant women.

Inclusion criteria

Paper I included only women with singletons who took part in the MoBa study once. **Paper II** and **Paper III** are based upon the same study population, but restricted to nulliparous women who were continent before pregnancy. To be able to explore incident UI in pregnancy or postpartum, women had to be continent before pregnancy. To explore associations between UI and pregnancy and labor, previous exposure to pregnancy and labor could elude associations. Nulliparous women who were continent before pregnancy represents the best clinical model of a pelvis unexposed to known pregnancy-related risk factors, and thereby the best population to assess the risk of UI

associated with pregnancy and delivery. Farrell recommended this study population for exploring associations between UI and pregnancy and delivery [Farrell 2001]. Before **Paper II** was published in 2009, not many studies had used these inclusion criteria [Eftekhar 2006, Thomason 2007]. An increasing number of studies on UI the latter years have started using these inclusion criteria [Arrue 2010, Solans-Domenech 2010].

Exposure data

Due to our large study population, we were able to categorize/stratify the exposure variables to a larger extent than usually found in comparable literature, and we have still power to calculate risk estimates with high degree of precision.

Most papers operate with two modes of delivery: CS and vaginal delivery [Turner 2009]. In **Paper II**, mode of delivery was categorized into elective CS, acute CS intended as elective CS, acute CS intended as SVD, SVD, vacuum and forceps delivery. No prior study has earlier presented mode of delivery – data like this. An unresolved research question has been whether or not there are different risks associated with the different CS groups. CS before or after the onset of labour are likely to affect the risk of UI differently. Women who are intended for elective CS are likely to be different from women intended for SVD [Chigbu 2007], independent of final mode of delivery. To understand the true effect of CS on UI, this type of potential confound by indication must be dealt with. In our study this confounding was reduced as we stratified mode of delivery in line with recommendation for future research on the association between CS and UI [Nygaard 2006]

In **Paper III** data was stratified for BMI groups. Both BMI and weight gain are risk factors for UI [Townsend 2007]. Initial weight when becoming pregnant is likely to affect how the women respond to weight change in pregnancy. In addition, there are different weight gain recommendations for the different BMI groups [Rasmussen 2009]. Previous studies on UI and weight change in

pregnancy have not stratified for BMI. Due to the large study population we were able to achieve narrow CIs even after stratifying for pre pregnancy BMI.

In **Paper III**, we used percentiles to categorize weight gain. We investigated how weight gain beyond the median affected UI; but to isolate the effects of extreme weight gain, we also analysed weight gain beyond the 90th percentile. Weight gain according to the Institute of Medicine's recommendations for weight gain in pregnancy [Rasmussen 2009] could have been used, but our main focus was not to investigating how the Institute of Medicine's recommendations affected UI. A recent study indicated that only 22 % of pregnant women gained weight according to the Institute of Medicine's recommendations [Gould Rothberg]. Percentage of weight change, BMI change, weight gain according to the US Institute of Medicine recommendations, and absolute weight change were explored. These methods led to the same patterns of results. We presented both absolute weight change in kilograms at the 50th and 90th percentiles and weight change as a continuous variable; as we found these methods appropriate for our study aim and easy to interpret. If an association between UI and weight gain existed, analyses on the 90th percentile would be likely to reveal the association.

Confounding

A confounding variable is an extraneous variable that correlates with both the dependent and the independent variable, and can thereby lead to wrong conclusions. To avoid a false positive (Type I) error researchers must control for confounders [Altman 2006].

The MoBa study aim at estimating associations between potential causal factors and ill health in mother and child. Exsposure data were obtrained through comprehensive data collection on factors such as diet, infections, hereditary factors, environmental toxins, medication, exposure to occupational hazards, lifestyle and previous disease, to mention some. This made it

possible to adjust for several important confounders. The linking of data to the MBRN registry made it possible to analyse objectively measured data registered during labour reported by health professionals. We performed analyses of confounding on birth variables like rupture degree 3-4, duration of labour, baby's weight, head circumference etc. In addition we did confounder analyses on established risk factors such as age, BMI, mode of delivery etc. Confounding was evaluated by a variable's effect on exposure and outcome and effect estimate. Possibilities for searching for potential confounding are almost infinite in the MoBa study. We focused mainly on available delivery and child variables as potential confounders. According to Dolan et al, few cohort studies on UI in pregnancy on primiparous women after delivery have used multivariate or logistic regression analysis to adjust for confounding variables [Dolan 2004]. However, variables found to be confounders in **Paper I** – **III** are in line with studies on UI in pregnancy who give an account for their use of confounder analyses [Dolan 2004, Farrell 2001, Glazener 2006]. The assessment of confounders was comprehensive and lead to improved accuracy of our effect estimates.

Still, some limitations regarding confounders must be addressed; pelvic floor muscle training was not investigated as a confounder, as these data were to be explored by a different research group. We did not have access to delivery variables concerning CS as phase, stage, fetal distress, trial of instrumental delivery ahead of CS. As mentioned under Chapter 1.8.2, there are numerous potential confounders that can be investigated.

We do not know all factors that are involved in the mechanism of UI. We can never rule out the possibility of rest confounding. However, when performing confounder analyses, only "established risk factors" (i.e. age, BMI, continence status in pregnancy and mode of delivery) appeared to affect exposure, outcome and effect estimate. The likelihood of any other confounder to substantially affect our UI estimates considerably appears to be small.

Internal validity

Internal validity refers to the extent to which we can accurately state that the independent variable produced the observed effect. According to Rothman's well recognised textbook "Modern epidemiology", major threats to internal validity are confounding, selection bias and information bias.

Information bias occurs due to mismeasurement of the variables studied. To find associations between exposure and outcome, exposure data must be valid. The MBRN data was quality tested and considered to have high accuracy. All filled-in questionnaires in MoBa were sent by mail to a central facility where they are registered, scanned and verified. Answers to specific questions were checked for logical content and consistency. Illegal values, values out of limit values and dependency rules are controlled. If the registered value in the databank was consistent with what the mother had written, the value was kept in the database even if it was absurd. Every scientist who works with the database must consider their limit values and define outliers.

In **Paper III** we have excluded data on weight, weight gain and height that were very likely to be inaccurate (Figure 5).

We did a descriptive statistic frequency test of height. We set the lowest cut-off for height at 1.40 m (this could be an average 13 year old at the 50 percentile weight curve and the 2.5 percentile height curve). We included the tallest women, reported to be 1.96 m.

We did a descriptive statistic frequency test of weight (Figure 5). We set a general cutoff at 40 kg. There were 6 women reporting pre pregnancy weight between 0-10 kg, 2 women reporting weight 11-30 kg, and 3 women reporting weight 31-40 kg. The heaviest women reported pre pregnancy weight of 160 kg. She was included.

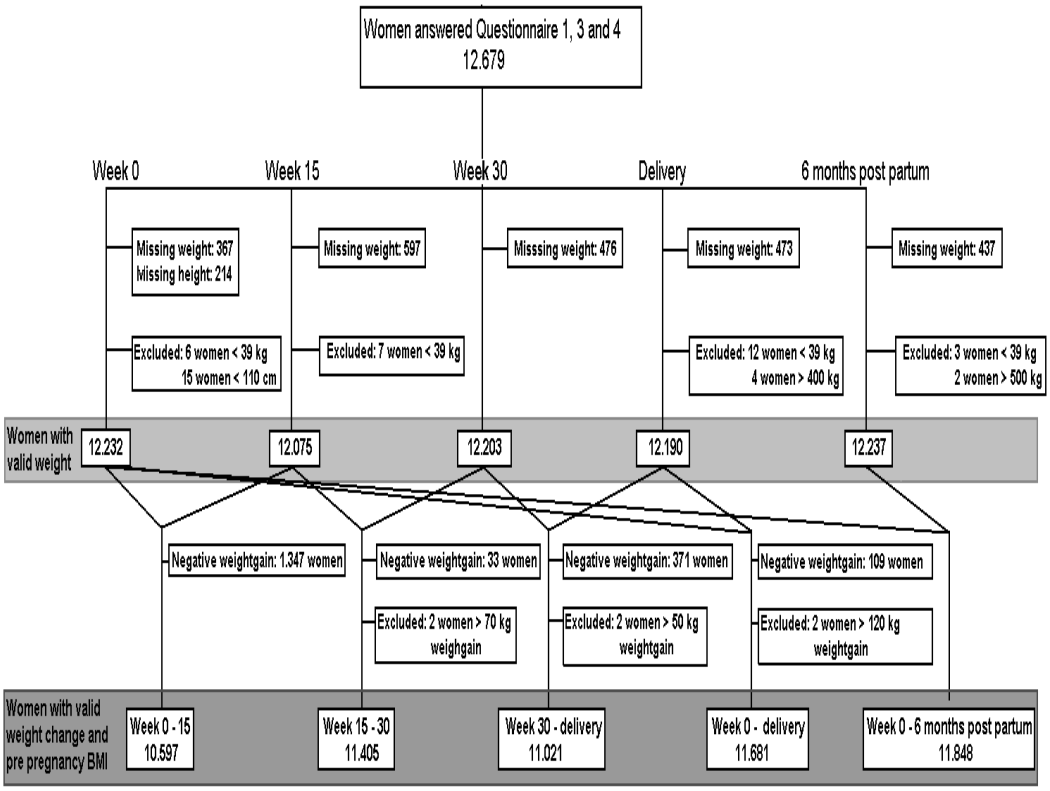
Several weight changes were excluded in analyses in **Paper III** (Figure 5). Women who reported weight loss during any time period in pregnancy were

excluded as well as women reporting impossible weight gain during a certain time period (i.e. reporting 60 kg before pregnancy and 670 kg in week 15 of pregnancy).

Analyses must be performed carefully to achieve internal validity. The UI research group has long experience with register data, SPSS and regression analyses. Co-authors have been involved in the analyses. We have performed confounder analyses and adjusted were appropriate to give a more accurate effect estimate of the association between exposure and outcome. We believe that the chosen measures adequately assess what the study intended to investigate.

We do not believe that information bias represent any threat to the internal validity in our study. Selection bias and confounding is discussed separately, and we concluded that they are likely not to represent a large threat to internal validity.

Figure 5. Included and excluded participants in study III



Publication bias

Articles with significant postive findings are more likely to be published than articles without such findings. In **Paper II** we did not find any significant differences in risk after SVD between women who were continent and incontinent in pregnancy, and we could thereby not point out a certain group who would benefit from CS based on continence status in pregnancy. In **Paper III** we could not identify weight gain in pregnancy as a major risk factor for neither UI in pregnancy nor postpartum. Despite so called “negative results” both papers were published in well recognized journals. Publication of negative results strengthens the evidence of these true null hypotheses.

Questionnaires

The questionnaires consisted of 14 – 16 pages with questions. Questions regarding UI totalled only a minor part of the questionnaire. It is unlikely that there was a selection bias due to UI in the MoBa data material.

UI was identified through questionnaire, not objective testing. Objective testing might reveal a different prevalence and incidence rate. Objective testing for UI is not recommended in epidemiologic research on UI. It would have been impossible to objectively test 100,000 pregnant women in week 15 and 30 for UI. The UI questions in MoBa are in accordance with the present definition of UI symptoms; “any complaint of involuntarily leakage of urine” [Haylen 2010].

The research group on UI in Bergen has earlier used the Sandvik’s severity index questions [Sandvik 2006]. These validated questions concern frequency and amount. The questions on frequency focus on monthly leakage, weekly leakage and daily leakage. The MoBa UI questions are not formulated exactly the same way as Sandvik’s severity index, but concerns the same categories of UI. Sandvik’s severity index question number 2, 3 and 4 on frequency have the same meaning as the UI question 1, 2 and 3 on frequency in MoBa. When it comes to amounts, Sandvik’s severity index operates with “Drops or little” or “More”. We use the scale “Droplets”, “Larger amounts”, which corresponds to these two groups. Many surveys have used the same frequency and/or amount wording in questionnaires, among others Eason [Eason 2004]. An additional problem regarding the frequency and amount questions is that each type of UI was followed by a question regarding frequency and amount (Appendix 6). A woman with stress and urge UI will end up with 3 different severity scores. It is thereby impossible to estimate a mean frequency and amount – score for any UI. The MoBa questions on UI are not optimal, and are not validated, but we think that the content of our amount and frequency brings up the same information as other validated questionnaires on this subject. We

do, however, not have any proof of this. As a result, frequency and amount data are used with cautions.

The timing of the questionnaires represents a weakness that has to be addressed. As women answered Questionnaire 3 in week 30 of pregnancy, we do not know the actual prevalence of UI just before delivery. The correct prevaelence of UI in pregnancy (at delivery) were thereby likely to be somewhat higher. We were also not able to investigate the association between weight gain during week 30 – delivery on UI in pregnancy. Practically, it would be very difficult to make all women answer a questionnaire just before or after giving birth.

Questionnaire 1 had only one question regarding UI (Appendix 5). This question did not give information on type or severity of UI. Questionnaire 3 (Appendix 6) answered in week 30 of pregnancy was therefore used to estimate UI before and during pregnancy. This might lead to incorrect data regarding UI before pregnancy. In Questionnaire 3 30,631 women reported being continent before pregnancy. Of these, only 65 women (0.2 %) reported having UI before pregnancy in Questionnaire 1. Data from Questionnaire 3 thus appears to correspond well with data from Questionnaire 1.

4.1.2 Methodological weaknesses

Recall bias

Even though MoBa is a prospective cohort study, the possibilities of recall bias ought to be addressed. The women were asked to recall UI and weight before the first pregnancy. Questionnaire 1, answered in week 15, asked “Did you have UI before pregnancy?”. Unfortunately, the questionnaire lacked information regarding stress UI, urge UI, mixed UI, frequency and amount. In Questionnaire 3 answered in week 30, the women were also asked about UI before pregnancy. These questions also gave information about type and

severity of UI. These data were used to calculate prevalence of UI before pregnancy. Viktrup found that women remember the onset of UI in association with pregnancy incorrectly 5 years after delivery [Viktrup 2001]. Pregnancy is a very special phase in a woman's life. Pregnant women are particular aware their own body, body changes and onset of symptoms in pregnancy. We believe that women in week 30 of pregnancy are capable of remembering whether or not they had UI before pregnancy, but we can not rule out underestimation of UI prevalence before pregnancy.

Weight before pregnancy and weight at delivery were reported retrospectively. However, one study indicated high correlation between recall of prepregnancy weight and actual prepregnancy weight, even many years after delivery [Tomeo 1999]. In addition, 6 months postpartum, there is high correlation between self-reported weight and documented weight in pregnancy [Oliveira 2004]. All Norwegian women have a pregnancy chart documenting weight before pregnancy and at the time of birth. Hence, data for weight at these 2 time points were easy for women to recollect.

Statistical analyses

As time passes by, research methods and statistical analyses develops and matures. In **Paper I** OR was used as risk estimate, as this was the effect estimate used in comparable articles. Prevalent conditions and large ORs will lead to a gap between OR and RR; the OR estimate will be higher than the RR estimate. It is common to interpret OR as RR, and therefore falsely interpret the risk as too high. RR is therefore the recommended risk parameter in studies with high prevalence in the unexposed group. RR is also the recommended risk parameter in cohort studies.

In **Paper II** we therefore presented both OR and RR. All OR and CI were converted to RRs and corresponding CI by use of the formula $RR = OR/((1 – P) + (OR \cdot P))$ [Zhang 1998]. In this formula, P is the prevalence of UI in the unexposed group.

In **Paper III** we further refined the methodology by log binomial regression analyses in STATA to estimate RR. Only RR was presented. There were large differences between OR and RR, but only tiny differences in RR estimates between the two ways of estimating RR. The three papers thereby have different ways of calculating effect estimates. Recent years there are published several articles on UI in pregnancy using RR as their effect measurement [Baydock 2009, Hantoushzadeh 2010]. It is a weakness that **Paper I**, II and **III** do not have similar risk analyses. We recommend presenting RR in future studies on groups with high prevalence of UI. Still, several recent studies with high prevalence of UI present high OR as risk parameters [Brown 2010, Diez-Itza 2010]. Some recent articles have however used hazard ratio (HR) [Solans-Domenech 2010].

In **Paper III**, we analysed weight change among all women, underweight women, normal weight women and overweight women. The association between weight change according to the 50th and 90th percentile and UI in week 30 was analysed for two different time periods. The association with UI 6 months postpartum was analysed for six different time periods. Analyses on weight loss from delivery – 6 months postpartum was in addition stratified for continence status in pregnancy during. A total of 44 regression analyses with 95 % CI was performed, statistical significant associations were stated when $p < 0.05$. Due to the number of analyses, we were likely to find at least two false significant findings. Retrospectively, we could have used Bonferroni method to avoid type I errors. Few articles about UI use Bonferroni; I was only able to identify 8 articles on UI, all with focus on urodynamics, which had performed Bonferroni analyses. Bonferroni is performed by considering the number k of null hypothesis (n=44) that are to be tested and the overall type 1 error rate p ($p < 0.05$) by ordering the p-values and comparing the smallest p-value to α/k. If that p-value is less than α/k, the hypothesis is rejected and analyses are done all over with the same α and test the remaining $k - 1$ hypothesis and compare the smallest one to $\alpha/(k - 1)$. This is done until the hypothesis with

the smallest p-value cannot be rejected. At that point all hypotheses that have not been rejected at previous steps are accepted.

Due to our large sample size, the majority of our p-values were < 0.01. However, many effect estimates in **Paper III** was small and several CI were close to zero, leading to p-values 0.05 < x < 0.01. It is thereby a chance of type I error. On the other hand, we found a trend in significant findings; were significant associations were identified in **Paper III**; both the 50th and 90th percentile analyses within a BMI group were generally significant. In addition, significant findings were generally in association within the same time period; that is week 0 – 15 and UI in pregnancy, and week 0 – 6 months postpartum, delivery – 6 months postpartum and UI postpartum. This increases the likelihood of our findings to not be exposed to type I errors in this respect.

Power

A study will try to achieve the highest possible power, so that if the null hypothesis is false, the CI will be narrow and p – value will tend to be small numbers [Rothman 1998]. Power was not calculated, as we had a given data set to work on. Our dataset was based on enrolled women in 2006. There was no reason to believe that we would lack power in our analyses. However, in stratified analysed; for instance on underweight women gaining weight > 90th percentile (n = 26 – 31), or on women who were continent in pregnancy and delivering by acute CS intended as elective CS (n = 4) an even larger study population might have helped us avoid a type II mistake (not finding significant associations and thereby not rejecting the null hypothesis).

4.2 Discussion of results

4.2.1 Paper I

In **Paper I** we investigated prevalence, incidence and risk factors for UI in pregnancy among all women in MoBa at the time.

Incidence and prevalence

Prevalence of UI before pregnancy was 26 %. A large cohort study from Australia has reported similar prevalence of UI among a general population of women aged 18 to 50 years, with 24 % [Chiarelli 1999b]. Mean age in our study population was 29.5 years. Prevalence of UI among women 30 – 34 years in the Norwegian Epincont study was 18 % [Hannestad 2000]. A wide range of prevalence figures has been presented among both nulliparous (5 – 39%) and parous (19 – 48%) women [Foldspang 1992, Hvidman 2002, Rortveit 2001].

Epidemiologic data are scarce on cumulative incidence of UI in pregnancy. Incidences of UI in pregnancy are in the range of 8 – 57 % (Table 1). We reported a cumulative incidence of 45% of any UI. A recent study on nulliparous women found a cumulative incidence rate of UI in pregnancy of 39 % [Solans-Domenech 2010].

In **Paper I** prevalence of UI in pregnancy was 56 % (48 % among nulliparous, 67 % among parous women). Prevalence of UI in pregnancy varies widely in previous studies, with figures ranging from 4 – 70 % among nulliparous women, and from 14 – 85 % among parous women [Francis 1960, Groutz 1999, Hojberg 1999, Hvidman 2002, Morkved 1999, van Brummen 2006b] (Table 2). Our prevalence estimate of 58 % of UI pregnancy distributed unevenly on three types of UI was based on real time report of symptoms in a large, unselected population, similar to figures reported in other prospective

studies of pregnant women [Burgio 1996, Chiarelli 1997, Raza-Khan 2006]. A recent study on UI in pregnancy is also in line with our findings: an Australian study found a prevalence of UI among nulliparous women in third trimester of 56 % [Brown 2010].

The increased prevalence of UI in pregnancy was mostly due to high incidence of stress UI and mixed UI. This is in line with findings in previous studies that have investigated impact of pregnancy on type of UI [Dolan 2004, van Brummen 2006b, Viktrup 1992]. Several studies on UI in pregnancy have reported data on stress UI only, with estimates between 9 – 85 % [Eason 2004, Francis 1960, Groutz 1999, Scarpa 2006, Viktrup 1992]. Our estimate of 32 % stress UI is in the middle of the published range.

Risk factors

Age, parity and BMI are three main risk factors for UI in younger women [Burgio 1996, Chiarelli 1999b, Foldspang 1992, Groutz 1999, Hannestad 2003, Hojberg 1999, Hvidman 2002, Rortveit 2001]. In **Paper I**, adjusted analyses showed that parity was the strongest risk factor for UI both before and during pregnancy, with OR ≈ 2 for parous women. This is in line with other studies [Chiarelli 1997, Foldspang 1999, Scarpa 2006]. Some authors have found a certain threshold for the number of deliveries as risk factor for UI [Faúndes 2001, Rortveit 2001]. Our findings support that the first delivery has the strongest impact on UI before a new pregnancy, but subsequent deliveries also add to the risk for UI. However, the association with parity was weaker among pregnant women, indicating that pregnancy itself becomes a more important risk factor for UI when pregnant.

4.2.2 Paper II

In **Paper II** we investigated incidence and prevalence of UI 6 months postpartum, and how UI in pregnancy and mode of delivery affected UI postpartum among primiparous women who were continent before pregnancy.

Incidence and prevalence

In cohort studies incidence of UI postpartum among primiparous women who were continent both before and in pregnancy varies from 0 – 26 % [Farrell 2001, Glazener 2006, Huebner 2010, Solans-Domenech 2010, Viktrup 1992]. The cumulative incidence of UI 6 months postpartum was 21%. Reasons for the high incidence may be lower CS rates and higher rates of instrumental vaginal delivery in our study compared to the other studies [Farrell 2001, Glazener 2006, Viktrup 1992]. Also, the threshold to label UI was low, as UI last month was used to define UI. Our cumulative incidence on UI after CS, SVD and instrumental delivery were, however, equal to other studies [Farrell 2001].

UI was reported by 31% (3,991/12,679) women 6 months after delivery. In a recent systematic review of UI during the first 3 months postpartum, the pooled prevalence of any postpartum UI was 29% (95% CI 27-30%) among primiparous women 3 months postpartum [Thom 2010]. Due to low response rate in MoBa, **Paper II** was not found eligible for this review. Our findings are, however, in line with the results of this review.

Mode of delivery

We found that 3,710 of 10,714 (35%) women had UI after vaginal delivery. Reported prevalence of UI among primiparous women after vaginal delivery varies between 20 – 31 % [Eason 2004, Schytt 2004]. Recent cohort studies [Borello-France 2006, Eftekhar 2006], as well as reviews [Turner 2009] found similar prevalence range. Reasons for our somewhat higher prevalence estimate might be the use of prospective study design and lower CS rates.

There is growing body of evidence documenting vaginal delivery as predictor of UI also later in life [Burgio 2003, Glazener 2006, Rortveit 2003a].

According to general criteria used to claim that a risk factor is established, vaginal delivery fulfills these criteria; there is a large significant risk increase of UI after SVD, indicating a clinically important association. SVD is a risk factor in different studies [Farrell 2001, Hannah 2004], in different study populations [2001, Kozak 2002] and in different study designs [Groutz 2004, Hvidman 2003]. There is to a large degree consistency in the literature; the risk factor is reproduced in different studies. But also in studies on UI and SVD, some results are unambiguous [Thomason 2007]. There is a dose response dependent relationship between UI and SVD [McKinnie 2005] (but results are diverging even in Nordic studies [Altman 2006]). There appears to be a causal relationship between SVD and UI, as SVD is biologically plausible to affect the pelvic floor. Our article adds to the existing documentation on SVD as a risk factor for UI postpartum.

There is an ongoing controversy about the effect of *assisted* vaginal delivery on UI [Schytt 2004] as results do not show a clear tendency towards increased prevalence of UI postpartum [Farrell 2001, Hvidman 2003, Rortveit 2003b]. A recent study on primiparous women found increased risk of UI after assisted vaginal delivery [Jundt 2010]. Unfortunately, MBRN has no further information on which instrumental delivery failed and resulted in non-elective CS, or at what stage of delivery non-elective CS was carried out. This kind of missing information is a limitation of this study.

A referee for **Paper II** claimed there existed no documentation on UI after non-elective CS intended as elective CS or non-elective CS intended as SVD. We have not been able do come across articles, neither before nor after our publication, that presents such data. To update clinicians we presented detailed data for non-elective CS by splitting this group in three (those who were intended to deliver vaginally, those who were intended to deliver by

elective CS and an unspecified group). There were, however, no significant differences between these groups. A recent study on primiparous women have looked into how CS among women who were a) not in labour, b) in labour but not pushing or c) in labour and pushing affected UI postpartum [Boyles 2009]. In line with our results, they found no significant differences between the groups.

Continence status in pregnancy

We found an OR of 3.5 for UI 6 months postpartum among women who had UI in pregnancy compared with those who were continent during pregnancy. When reanalysing available data in previously published articles for comparison, ORs for UI postpartum among primiparous women by continence status in pregnancy vary from 2.5 to 9.2 [Foldspang 2004, Fritel 2004, Glazener 2006, Groutz 2004, Schytt 2004, van Brummen 2007, Viktrup 1992, Wilson 1996]. We identified six studies investigating the relationship between continence status in pregnancy and continence status postpartum in previously *continent* primiparous women, showing ORs of 1.7 [Glazener 2006], 1.9 [Viktrup 1992], 2.0 [Wilson 1996], 3.7 [Arrue 2010] and 5.8[Diez-Itza 2010], and 7.8 [Groutz 2004] (Table 6). There was no possibility for adjustments of OR in our reanalyses. Several new articles show that UI in pregnancy is an important predictor for UI both postpartum [Arrue 2010, Diez-Itza 2010, Wang 2010] and later in life [Altman 2006, Burgio 2003, Fritel 2004, Hvidman 2003, Schytt 2004, van Brummen 2006a, van Brummen 2007, Viktrup 2006].

Mode of delivery and continence status' association with UI postpartum

In Breslow-Day analyses we found no significant difference in risk for UI postpartum after CS compared to SVD among women who were continent or incontinent in pregnancy. Glazener et al [Glazener 2006] was the only research group identified investigating nulliparous women who were continent before pregnancy, stratified for continence status in pregnancy and then analysed delivery parameters with the same approach as we used. For

comparison, we set CS as reference group in Glazener's study and any CS as reference group in our material. Reanalysed this way, the OR for UI after vaginal delivery among women who were continent in pregnancy was 3.6 in Glazener's study and 3.3 in **Paper II**. Among women who were incontinent in pregnancy, the ORs were 2.6 and 2.6, respectively. Although Glazener et al used a retrospective design with data collection 3 months postpartum, our findings correspond very well with their results.

Although there was no statistically significant difference in RR reduction between groups, there was still a large difference in absolute risk reduction (-15% vs. -31%) (Table 8). However, RR is a better and more correct measure of risk in this study. It is an adjusted estimate, taking confounding into account. In addition, Breslow-Day test can be applied when comparing RR to see if the risk estimates are significantly different.

Table 8. Number (N), percentage and adjusted OR and RR for urinary incontinence 6 months postpartum by delivery mode, stratified for continence status in pregnancy.

	Continent in pregnancy					**Incontinent in pregnancy**				
	N	**%**	**OR**	**RR**	**CI**	**N**	**%**	**OR**	**RR**	**CI**
Elective CS	18	8	1	1	Ref	25	20	1	1	Ref
Acute CS intended as elective CS	4	13	1.6	1.4	0.4-4.1	3	21	1.4	1.3	0.3-2.9
Acute CS intended as SVD	66	8	1.0	1.0	0.6-1.7	153	30	1.9	1.6	1.1-2.2
Unspecified CS	3	8	0.7	0.7	0.2-2.8	8	29	2.0	1.7	0.7-2.8
SVD	1,166	23	3.9	3.2	2.1-4.7	1,837	51	5.5	2.9	2.3-3.4
Vacuum	250	26	3.9	3.2	2.1-4.6	337	56	6.4	3.1	2.4-3.6
Forceps	55	30	5.5	4.0	2.6-5.8	58	50	4.9	2.8	2.0-3.4

CS = cesarean section, SVD = spontaneous vaginal delivery, OR = odds ratio, RR = relative risk, CI = confidence intervals.

4.2.3 Paper III

In **Paper III** we investigated how weight gain and weight loss in association with pregnancy was associated with UI 6 months postpartum among primiparous women who were continent before pregnancy. The subject was surprisingly timely in the light of an increasing number of reviews the last two years concerning weight and UI.

Weight gain and UI in pregnancy

Weight gain between week 0 – 15 of pregnancy was associated with UI in week 30 of pregnancy, while weight gain between week 15 – 30 showed no such association. Other studies have also found no statistically significant association between total weight gain in pregnancy and UI before delivery [Eason 2004, Kristiansson 2001, Sottner 2006] (Table 7). A recent Spanish study on 478 primiparous women confirms these findings [Diez-Itza 2009]. No studies have investigated the effect of weight gain during different trimesters on UI, and only two articles on weight and UI in pregnancy present adjusted analyses [Diez-Itza 2009, Eason 2004].

Weight gain and UI postpartum

Weight gain in pregnancy did not affect UI 6 months postpartum. This made the association between weight gain during week 0 – 15 and UI in pregnancy less likely to be clinically important. This is in accordance with other studies. Eason et al [Eason 2004] found no increased risk for UI 3 months postpartum among women who gained > 17 kg in pregnancy compared to women who gained < 11 kg. A study from 2010 [Diez-Itza 2010] found no association between total weight gain in pregnancy and persistent UI 1 year postpartum. Our results were contrary to an Italian study [D'Alfonso 2006]. We reanalysed their data and found an unadjusted RR of 2.0 for UI 3 weeks postpartum among women who gained ≥ 15 kg in pregnancy. These articles did not stratify

for pre pregnancy BMI nor clarified their use of weight groups [D'Alfonso 2006, Eason 2004, Kristiansson 2001, Sottner 2006]. Our findings were also in contrast to results for weight gain in a cohort of non-pregnant women in The Nurses Health Study [Townsend 2007]; reporting an OR of 3.5 for frequent UI in a general population of women who gained more than 20 kg over a four year time period.

There were significant associations between high weight gain from before pregnancy through 6 months postpartum and having UI at 6 months postpartum. This weight gain represents mainly adiposity and not fetus, uterus etc. Recent years there have been published several reviews concerning weight and UI [Bart 2008, Greer 2008, Hunskaar 2008, Khong 2008, Subak 2009]. There is strong evidence, both in cross sectional studies and cohort studies, that increasing BMI is a risk factor for UI in general. These reviews do not concern weight gain during or after pregnancy, but our study in general adds to the existing literature concluding that increased adiposity is associated with UI. It has to be added that the findings of only minor association between weight gain in pregnancy and UI are not in line with the existing literature on high BMI and UI (See chapter 1.8.2).

Weight loss and UI postpartum

There was a decreased risk of UI 6 months postpartum by weight loss from the time of delivery – 6 months postpartum, both among women who were continent and incontinent in pregnancy (Table 9). One study of non-pregnant women have found similar association with weight loss as our study; an RCT study reported that 7% of overweight women with frequent UI became urinary continent after a mean weight loss of 7.8 kg over a 6 month period [Subak 2002]. Several reviews have been published the recent years regarding weight loss and UI [Altman 2009, Hunskaar 2008, Khong 2008, Natarajan 2009]. We have not, however, identified any study looking into the effect of weight loss postpartum on UI.

Table 9. RR of UI 6 months postpartum among primiparous women in Norway who were incontinent or continent in pregnancy, by weight loss from delivery – 6 months postpartum. Data are given for the total study group, and weight gain is categorized by 50 and 90 percentiles.

		Incontinent in pregnancy				**Continent in pregnancy**			
Percentile	Weight loss (kg)	N	Prevalence UI (%)	Adjusted RR	95% CI	N	Incidence UI (%)	Adjusted RR	95% CI
1 – 50	0 – 14.0	2,520	1,283 (51)	Ref		3,549	815 (23)	Ref	
51 – 90	14.1 – 21.0	1,807	825 (46)	0.9	0.8, 0.9*	2,882	549 (19)	0.8	0.7, 0.9*
> 90	≥ 21.1	419	157 (38)	0.7	0.6, 0.8*	643	118 (18)	0.7	0.5, 0.8*

Obstetricians have several potential efficient methods to reduce UI after delivery; minimising forceps deliveries and episiotomies, by allowing passive descent in the second stage, and by selectively recommending elective CS [Handa 1996]. However, pregnant women are most often recommended pelvic floor muscle training to prevent UI. Women suffering from UI in association with pregnancy are in general not informed about any other ways to achieve continence.

A recent study based on primiparous women in the MoBa study found that 57 % of the participants did pelvic floor muscle training ≥ 1 pr week in week 30 of pregnancy [Bo 2009]. A recent RCT found a RR of 0.8 for UI 3 months postpartum after pelvic floor muscle training compared to no training [Mason 2010]. A Cochrane review on pelvic floor muscle training in association with pregnancy found that pregnant women without prior UI who were randomised to intensive pelvic floor muscle training in pregnancy were less likely than women randomised to no pelvic floor muscle training to report UI 6 months postpartum (RR 0.7) [Hay-Smith 2008]. Women with persistent UI 3 months postpartum who received pelvic floor muscle training, 30 % less women reported UI 12

months postpartum compared to women who did not receive treatment (RR 0.79) [Hay-Smith 2008]. In **Paper III** we found a risk reduction (RR 0.7) for UI 6 months postpartum after weight loss > 90th percentile from delivery to 6 months postpartum both among women who were continent and incontinent in pregnancy. In other words, the effect of weight loss found in our study is in line with the effect of pelvic floor muscle training. It should be commented that a large weight loss postpartum could imply substantially more effort than pelvic floor muscle training. We believe that the associations between UI and weight loss postpartum in our study are of clinical importance. Weight loss should therefore be considered as a possible addition to pelvic floor muscle training. Weight loss postpartum, together with pelvic floor muscle training [Hay-Smith 2008, Morkved 1997, Morkved 2000], may decrease the prevalence of women with UI postpartum.

5. Conclusion

5.1 Paper I

The prevalence of UI increases substantially in pregnancy; the prevalence increased from 26% before pregnancy to 58% in week 30. The cumulative incidence was 46%. Incontinence both before and in pregnancy seems to be associated with parity, age, and body mass index.

5.2 Paper II

UI was reported by 31% of the women 6 months after delivery. The cumulative incidence was 21 %. Women who were continent in pregnancy had statistically significant lower prevalence of UI postpartum compared with women who were incontinent. Elective CS was associated with less risk of UI postpartum compared to SVD. There were, however, no statistically significant differences in risks between women who were continent and incontinent in pregnancy depending on mode of delivery. Our findings indicate that the association between mode of delivery and continence status postpartum was not influenced by incontinence status in pregnancy. Prediction of a group with high risk of UI according to mode of delivery cannot be based on continence status in pregnancy.

5.3 Paper III

Weight gain in pregnancy was of little relevance to continence status in pregnancy and postpartum, and can therefore not explain the high prevalence of UI in pregnancy among nulliparous women. High weight gain from start of pregnancy through 6 months postpartum was the only weight-associated risk factor for UI 6 months postpartum. Weight loss postpartum seems to be important for regaining continence and avoiding UI 6 months postpartum, and should therefore be addressed during continence promotion. Our findings can

help urinary incontinent women with continence instructions beyond pelvic floor training by encouraging them to loose weight after delivery.

6. Implications

Researchers ought to be careful not to exaggerate the clinical implications of their research results. The following implications of **Paper I – III** may be anticipated:

6.1 Implications

The results in **Paper I** may contribute to increased focus on UI during pregnancy as a highly prevalent condition. **Paper II** may be a contribution to the discussion of CS to prevent UI. I have the highest anticipations for **Paper III**. The results may lead to awareness of weight loss post partum as an important conservative way of continence promotion.

6.2 References to own research

It usually takes time for an article to reach recognition and to be cited. Few articles become frequently cited reference articles. By using ISI Web of Knowledge number of citations for each article can be found. In addition, referral to my papers has been identified when reading articles.

All 3 papers are published in recognized journals of their kind. **Paper I** was published in “Obstetrics and Gynecology”; the international obstetric journal with the highest impact factor (4.4, 2009). **Paper II** was published in “British Journal of Obstetrics and Gynecology”; the second highest rated international obstetric journal with an impact factor (3.4, 2009). **Paper III** was published in “American Journal of Epidemiology”; the international epidemiology journal with the highest impact factor (5.6, 2009).

6.2.1 Citations Paper I

Paper I was published in 2007. Recent years it has been cited in several articles as an important reference article on UI in pregnancy. By June 2011 **Paper I** had been cited in 21 articles during the last 4 years [Adaji 2010, Al-Mehaisen 2009, Arrue 2010, Brown 2010, Diez-Itza 2009, Fiadjoe 2010, Herbruck 2008, Kawaguchi JK 2010, Kim 2007, King 2010, Klemetti , Kocaoz 2010, Lukasse 2009, Marecki 2010, Martins 2010, Mason 2010, Milsom 2009, Panayi 2009, Sharma 2009, Solans-Domenech 2010, Thom 2010]. **Paper I** has also been self cited in **Paper II** and **Paper III**.

Paper I has been frequently cited both in the introductions and discussion sections in articles regarding UI in pregnancy [Adaji 2010, Arrue 2010, Brown 2010, Kim 2007, King 2010, Kocaoz 2010, Marecki 2010, Martins 2010, Mason 2010, Solans-Domenech 2010]. Several of these articles highlight results from **Paper I** in the text, and refer to **Paper I** as the largest comparable article [Milsom 2009]. Many of the above articles compare their findings to **Paper I**, and conclude that their results are in line with our results [Arrue 2010, Brown 2010, Martins 2010, Mason 2010]. Due to different inclusion criteria, one study concluded that their figures of UI in pregnancy was not line with our findings [Adaji 2010].

Some articles refer to **Paper I** regarding BMI, age and parity as risk factors for UI [Adaji 2010, Arrue 2010, Brown 2010, Fiadjoe , Kim 2007, King 2010, Kocaoz 2010, Marecki 2010, Martins 2010, Mason 2010, Solans-Domenech 2010]. They in general conclude that these risk factors must be considered “established”, and further research on these risk factors are probably not needed.

Due to the size of the study population, the quality and the interest so far, hopefully **Paper I** will be a frequent cited article in UI research in pregnancy in the coming years.

6.2.2 Citations Paper II

Paper II was published in 2009. By May 2011 the article had already been cited 11 times; [Arrue 2010, de Souza Santos 2010, Diez-Itza 2010, Fritel 2010, Golding 2009, Humburg, Martins 2010, Menezes 2010, Okamoto 2010, Solans-Domenech 2010, Thom 2010].

Paper II has been most cited in regards of UI prevalence postpartum [Martins 2010, Solans-Domenech 2010, Thom 2010]. Figures in these recent articles are in general in line with our findings. However, our UI incidence estimates postpartum in one article differs from this article (21% vs. 9%) [Solans-Domenech 2010], probably due to different CS rates in the study population.

Several citations refer to **Paper II** regarding UI in pregnancy as a risk factor for UI postpartum [Arrue 2010, Diez-Itza 2010, Menezes 2010]. The latter to articles concluded that UI in pregnancy was the only independent risk factor for UI postpartum. Our RR increase for UI postpartum among women with UI in pregnancy compared to women without UI in pregnancy was in line with these recent articles.

Paper II is a very large cohort study looking into the association between mode of delivery and UI postpartum. Therefore, several articles refer to **Paper II** in this regard [Diez-Itza 2010, Fritel 2010, Solans-Domenech 2010]. The latter article also refers to **Paper II**'s focus on the effect of instrumental delivery.

Only one article has cited us regarding the conclusion; association between UI in pregnancy and mode of deliver on UI postpartum [Menezes 2010].

6.2.3 Citations Paper III

Paper III was published in 2010, six months before this text was written. **Paper III** has yet to be cited. However, the abstract publication of **Paper III** from ICS

2009 has been cited once [Cartwright 2009]. The author gives a brief summary of our article, and concludes “Post-partum weight loss should be encouraged on the basis of these data.”

6.2 Future research

During my time as researcher, I have been thinking of both possible and impossible research projects on UI. As RCT studies indeed reach Level 1 of evidence while cohorts reach Level 2; it could be interesting to do a the following hypothetical experiments:

- Randomise women to SVD or CS to find the true association with UI postpartum.
- Randomise women at delivery to “weight loss” or “no weight loss” to find the true association with UI postpartum.
- Randomise women at fertilization to “weight gain” and “no weight gain” in pregnancy to separate pregnancy as a risk factor from weight gain as a risk factor.

All three experiments would of course be hypothetical and impossible to perform and highly unethical. Level 2 of evidence will thereby maybe be the best possible evidence to these research questions.

Our conclusion in **Paper II** and **Paper III** ought to be in line with future research, and consistency in the literature must exist before our results might one day will be part of so-called established risk factors. Research in different setting, different populations and including not only nulliparous women would add knowledge and external validity to future conclusions.

There are still many unresolved research questions regarding weight, weight change and UI. As written in Chapter 1.8.2; there are many interesting factors

surrounding weight and UI that has yet to be investigated. There is need for prospective studies, preferably lifelong studies, investigating the duration of weight and weight gain's association with incident UI. Validated questionnaires should be used. We need to know whether weight represents it muscles, pregnancy, oedema or body fat? The study should compare waist-hip-ratio, waist circumference, total body fat and visceral fat to find the best parameter to be associated with UI. The study should have data to control for other diseases, hormonal changes, social characteristics and distinguished food intake. Studies should try to determine how these factors influence UI, and how they affect the association between weight and UI. Analyses in future studies on weight and UI should differentiate between the types of UI. I believe future studies will bring on new interesting information to change the established truths on weight and UI.

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Appendix

1. **Paper I**
2. **Paper II**
3. **Paper III**
4. MBRN
5. MoBa Questionnaire 1
6. MoBa Questionnaire 3
7. MoBa Questionnaire 4